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Laurence S. Reisner, MD, *Guest Editor*

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Contributors

JOANNA BROWN SULLIVAN, MD, Assistant Professor of Clinical Anesthesia, University of California, San Francisco, San Francisco, California

CATHY JO CANTRELL, MD, Assistant Clinical Professor, Department of Reproductive Medicine, Division of Perinatal Medicine, University of California, San Diego, San Diego, California

H. S. CHADWICK, MD, Associate Professor, Department of Anesthesiology, University of Washington, Seattle, Washington

DAVID H. CHESTNUT, MD, Associate Professor of Anesthesia, Obstetrics and Gynecology, University of Iowa College of Medicine, Iowa City, Iowa

RICHARD B. CLARK, MD, Professor, Departments of Anesthesiology and Obstetrics and Gynecology, University of Arkansas for Medical Sciences; Director, Obstetric Anesthesia, University Hospital, Little Rock, Arkansas

MARY JO A. CURRAN, MD, Attending Physician, Director of Obstetric Anesthesia, Michael Reese Hospital and Medical Center; Assistant Professor of Anesthesiology, University of Illinois, College of Medicine, Chicago, Illinois

RONALD DWORKIN, MD, Staff, Department of Anesthesiology, Greater Baltimore Medical Center, Baltimore, Maryland

HAROLD J. HEYMAN, MD, Clinical Professor, Department of Anesthesiology, University of Illinois College of Medicine; Director of Obstetric Anesthesia and Coordinator, Residency Education, Illinois Masonic Medical Center, Chicago, Illinois

STEPHANIE A. HUGHES, MD, Chief Resident, Department of Anesthesiology, University of California, San Diego Medical Center, San Diego, California

ESTHER C. JANOWSKY, MD, Assistant Research Professor of Anesthesiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

THOMAS G. KARAGIANES, MD, Assistant Clinical Professor, Department of Anesthesiology, University of California, San Diego, School of Medicine; Associate Director, Surgical Intensive Care Unit, University of California, San Diego Medical Center, San Diego, California

ROBERT B. LECHNER, MD, PhD, Assistant Professor, University of Virginia, Charlottesville, Virginia

CRAIG H. LEICHT, MD, MPH, Director, Obstetric Anesthesia, U.S. Naval Hospital and Medical Center, San Diego, California

WALTER L. MILLAR, MD, Associate Clinical Professor of Anesthesiology, University of California, San Diego; Staff Anesthesiologist, Anesthesia Service Medical Group, Inc., San Diego, California

FRANK C. MILLER, MD, Professor and Chairman, Department of Obstetrics and Gynecology, University of Arkansas for Medical Sciences; Chief of Staff, University Hospital, Little Rock, Arkansas

BRIAN L. PARTRIDGE, MD, DPHIL, Assistant Professor of Anesthesiology, University of California, San Diego Medical Center and San Diego VA Medical Center, San Diego, California

KENNETH L. POLLACK, MD, Fellow in Obstetric Anesthesia, University of Iowa Hospitals and Clinics, Iowa City, Iowa

LAURENCE S. REISNER, MD, Professor of Clinical Anesthesiology and Reproductive Medicine, University of California, San Diego; Vice-Chair, Department of Anesthesiology, Director of Obstetric Anesthesia, University of California, San Diego Medical Center, San Diego, California

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Preface

LAURENCE S. REISNER, MD
Guest Editor

In past years, the overhead loudspeaker call of "Anesthesia to delivery room one, STAT!" was frequently the method by which anesthesiologists were first introduced to their obstetric colleagues and their patients. Such an introduction often sent terror through the anesthesiologist's heart as he started off toward unknown problems and uncertain dangers. Fortunately for all concerned, this scenario is on the decline. Obstetric anesthesia is now a recognized subspecialty discipline and virtually all anesthesiology residents receive training in this field. Obstetric anesthesiologists work quite closely with the obstetrician, the parturient, the neonatologist, and the obstetric nurse to ensure proper and appropriate care for both mother and infant. This level of communication and information exchange is critical to providing the highest possible level of care and absolutely essential to the management of the high-risk pregnancy. The anesthesiologist who functions as a valuable consultant member of the obstetric health care team is familiar with the physiologic changes of pregnancy and their influence on disease states, the process of parturition and the potential problems lurking therein, and the specific disorders of pregnancy as well as the knowledge and skills inherent in the practice of anesthesiology.

This issue of *Anesthesiology Clinics of North America* deals with some of the current topics of interest in obstetric anesthesia. The reader, whether a full-time obstetric anesthesiologist or an occasional participant will find that although many of the topics are familiar, new and often controversial viewpoints are presented. Included in this volume are updates on the pharmacology of local anesthetics with a focus on obstetric usage, the tocolytic agents, the oxytocic drugs, and the prostaglandins used in obstetric practice today. Each of these is of special interest to the anesthesiologist as they have a significant influence on anesthetic administration and potential drug interactions. The use of systemic analgesics for labor analgesia is still utilized for approximately 50% of laboring patients. Is this appropriate? Epidural analgesia is certainly no longer considered a unique luxury. Appropriate techniques and subtle modifications are explored and discussed in this issue. The pregnant patient who must present for surgery during gestation is a particularly vexing situation. What, if any, is the correct anesthetic approach? How should this patient be monitored? Which drugs should be avoided? The preeclamptic patient may suffer from multiorgan failure. What should we look for? Which anesthetic technique is most appropriate for cesarean section? How do we control blood pressure? The introduction of spinally administered opiates has provided anesthesiologists with a wealth of opportunities to participate in the postoperative care of patients. This has been especially true for the post-cesarean section patient who desires a rapid recovery and an opportunity to enjoy her newborn and her family while in the hospital. Approaches to providing postoperative analgesia are explored in this edition as well as a review of post-cesarean section complications. The pregnant patient with serious medical disease requires expert critical care management. The reader is presented with the essentials of such care and the interpretation of laboratory and physical findings as they are influenced by both the physiologic changes of pregnancy and the medical illness. The final article yields the most current information on the acquired immune deficiency syndrome, the modern plague that incredibly, has already invaded the obstetric suite. Management of these patients requires special consideration for the parturient, the infant, and the health care providers themselves. These questions, issues, controversies, and frontiers are discussed by highly qualified, actively practicing physicians in their respective fields.

I am confident that the reader will find the information presented here more than just a repetition of prior knowledge and useful in clinical practice. I wish to express my great appreciation to the authors who have organized and presented the material in this volume while maintaining their busy practices. I also thank Margaret Burns, the editor of this series, for her kind words of reassurance and guidance during the preparation of this issue. Finally, I thank the pioneers in obstetric anesthesia for the dedication and persistence that has brought the anesthesiologist into the delivery suite on a permanent basis.

LAURENCE S. REISNER, MD
Guest Editor

Professor of Clinical Anesthesiology and Reproductive Medicine
University of California, San Diego
225 Dickinson Street
San Diego, CA 92103

Foreword

Obstetric anesthesia in the United States has undergone an exciting evolution through the last three decades. Initially a subspecialty engaged in by just a dedicated few, it has emerged as an integral part of the practice of most anesthesiologists. Indeed, the anesthesiologist is now considered by all to be an essential member of the obstetric care team.

Through this period of increasing importance and emergence, we have learned a great deal about maternal and fetal physiology and the effects of anesthesia on both of these patients. We have gained insight into the hypertensive disorders of pregnancy and have been instrumental in advancing the critical care of these patients. The last 10 years have witnessed a significant increase in our knowledge of local anesthetic pharmacology and neurotoxicity. The CNS action of opioids has been elucidated and applied to both labor analgesia and post-cesarean section pain management. Our obstetric colleagues continue to challenge us with the systemic effects of new uteroactive drugs, e.g., the tocolytics and the prostaglandins and a new disease, autoimmune deficiency syndrome, has appeared to challenge us all. Our knowledge and our anesthetic techniques (both regional and general) have evolved into an era of fine-tuning our approach to the obstetric patient, both normal and high-risk, to provide the optimal care for both the mother and her infant. This issue incorporates this information and is, therefore, a timely update and perspective of current obstetric anesthesia and perinatal medicine by actively involved experts.

Laurence S. Reisner, MD, the guest editor of this issue of *Anesthesiology Clinics* is especially qualified as an editor in this field. He began his medical career as an obstetrics and gynecology resident and evolved, several years later, into an anesthesiologist with a primary interest in obstetric anesthesia. Vested in both specialties, he has been a very able director of obstetric anesthesia training programs during the past 15 years. His excellent obstetric anesthesia service at UCSD is coupled to an outstanding reproductive medicine program; these divisions have a high degree of mutual respect and interact in such a manner as to provide excellent care for a parturient population that has a high proportion of high-risk patients. The excellent clinical care is paralleled by excellent teaching and contributions to the anesthesiology literature. Through his many anesthesia and obstetric associations he has come to know those who both best practice and teach the art and science of obstetric anesthesia. These actively involved physicians are the authors of the articles in this issue. Thus, both the subject matter at hand and the expertise of the editor and the authors make "Obstetric Anesthesia" a very compelling issue of *Anesthesiology Clinics* to read.

JONATHAN L. BENUMOF, MD
Consulting Editor

Professor
Department of Anesthesia
University of California, San Diego
Anesthesia Research Laboratory, T-001
La Jolla, CA 92093

0889–8537/90 $0.00 + .20

Pharmacologic Aspects of Local Anesthetic Use

*Esther C. Janowsky, MD**

THE NERVE

Impulse Transmission

Local anesthetics (LA) are extremely useful agents in clinical medicine because of their ability to temporarily interrupt the transmission of nerve impulses. The nerve membrane is the structure most important for transmission of nerve impulses; it separates the axoplasm, a milieu rich in potassium (K^+) from a sodium (Na^+) rich environment, the extracellular space. Because of these ionic gradients, an electrochemical potential of approximately −90 mV exists across this membrane with the interior of the cell being negative with respect to the exterior. In this state, the nerve is polarized (Fig. 1). Details of transmembrane ionic movements are discussed elsewhere.[78]

Impulse blockade by LA occurs by selective inhibition of sodium channels (Fig. 2). The normal function of the channel is interrupted primarily because it cannot open during a depolarization. Sodium channels, potassium channels, and even calcium channels are inhibited by traditional LA. This lack of selectivity diminishes the impulse-blocking potency of local anesthetics; to the extent that a drug blocks K^+ channels in addition to Na^+ channels, it is less potent than if it blocked Na^+ channels alone.[78]

Differential Blockade

Mammalian nerve fibers are grouped into three categories, based on fiber size and conduction velocity (Table 1).

Traditionally, sensitivity to LA was thought to be inversely related to fiber size. Newer studies have caused some rethinking of this view. Recent investigations of the in vitro sensitivities to local anesthetic block of A, B, and C fibers in rabbit vagus nerves have consistently

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*Assistant Research Professor of Anesthesiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

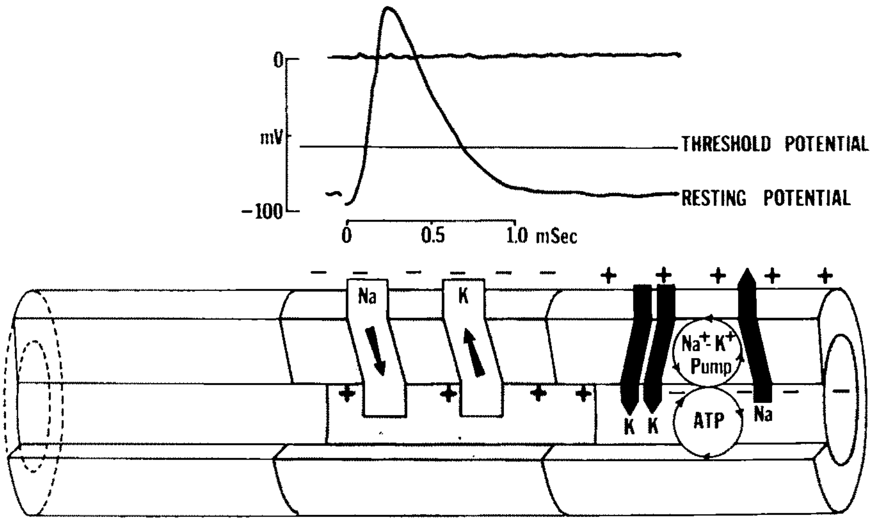


Figure 1. Relationship between membrane action potential and ionic flux across the nerve membrane. (*From* Covino BG, Vassallo HG: Local Anesthetics, Mechanisms of Action and Clinical Use. Grune & Stratton, 1976; with permission.)

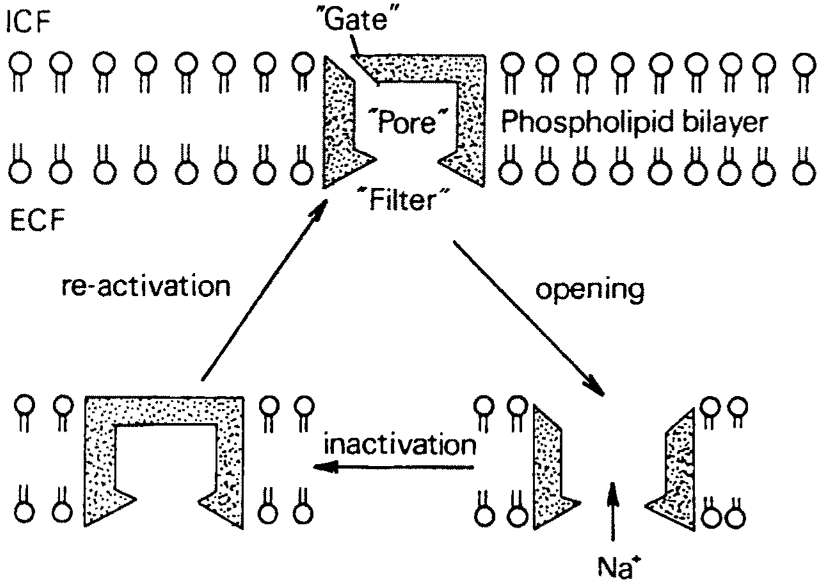


Figure 2. Functional components and possible "states" of a sodium channel. (*From* Wildsmith JAW: Peripheral nerve and local anaesthetic drugs. Br J Anaesth 58:692–700, 1986; with permission.)

Table 1. *Categories of Mammalian Nerve Fibers*

		FIBER DIAMETER (μ)	CONDUCTION VELOCITY (m/sec)	TYPE AND FUNCTION
A				
	α, β, γ, δ	1–22	10–120	Myelinated motor proprioception sensory
B		1–3	10–20	Myelinated autonomic
C		0.3–1.3	0.5–2	Unmyelinated autonomic sensory

demonstrated that A fibers are the most and C fibers the least sensitive to blockade by local anesthetic agents (Fig. 3).[37, 38, 83] Equipotent concentrations of esters and amides block C fibers at approximately the same rate, but the absolute and relative rates of development of A fiber blockade are related to lipid solubility; agents with greater lipid solubility block A fibers at a more rapid rate than agents of lesser lipid solubility. Rate of onset of block appears faster in slow-conducting fibers, probably because there is less of a diffusion barrier surrounding the smaller fibers; this reflects what is usually seen clinically. At steady-state equilibrium block, intrinsic nerve membrane sensitivity to the blocking action of LA is greater in fast fibers because

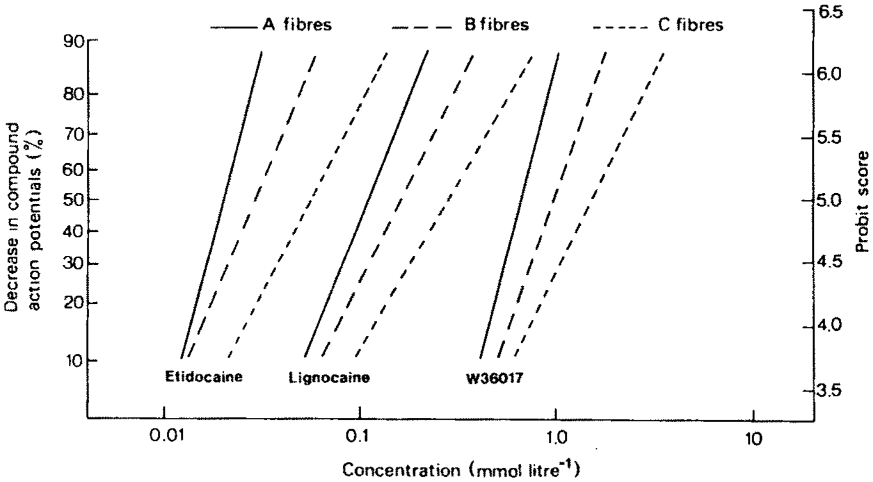


Figure 3. Dose-response relationships for the effect of three amide local anesthetics (lidocaine and two analogues) on three fiber types. Desheathed rabbit vagus in vitro; carbonated Liley solution; 23 to 26 °C; pH 7.4. (*From* Wildsmith JAW, Gissen AJ, Takman B, et al: Differential nerve blockade: Esters vs. amides and the influence of pK_a. Br J Anaesth 59:379–384, 1987; with permission.)

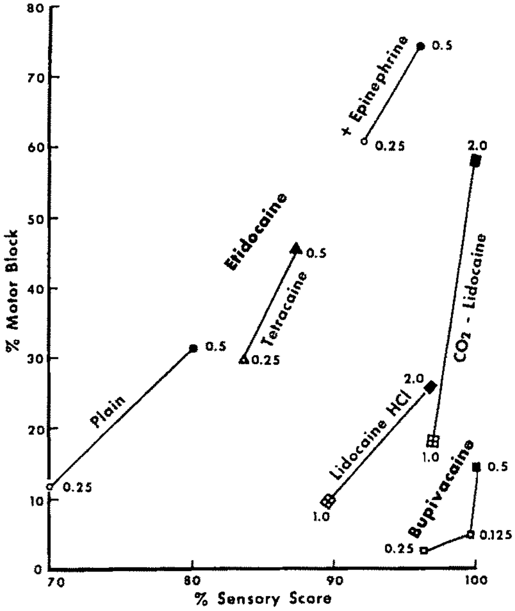


Figure 4. Epidural analgesia in labor. Quality of sensory and motor blockade with various analgesic solutions. Each point is the mean of 20 to 50 cases. Note the dissociation between intensity of motor and sensory blockade with the four agents tested and the most favorable ratio of sensory to motor block with bupivacaine. (*From* Bromage PR: Epidural Analgesia. Philadelphia, Saunders, 1978; with permission.)

of a lower margin of safety for transmission.[37] Furthermore, the relative position of the fiber in nerve bundles will provide rapid or slow exposure to blocking concentrations of LA. The ideal agent for obstetric anesthesia would include among many other properties the ability to create a high quality of analgesia with minimal motor block; bupivacaine in low concentrations approaches this ideal (Fig. 4).

Pregnancy and Nerve Function

Pregnancy may affect nerve sensitivity to LA.[28] The time required for 50% depression of the action potential of A, B, and C vagal fibers from pregnant and nonpregnant animals was determined after the application of bupivacaine (Fig. 5). Onset time for conduction blockade in each type of nerve fiber was faster in fibers from pregnant as opposed to nonpregnant animals and the differences were highly significant. In addition, preliminary findings suggest a slowing of nerve conduction velocity in humans with the progression of pregnancy.[77] An animal study has demonstrated a significant reduction in A-fiber conduction velocity during pregnancy but not in that of B or C fibers.[28] Mechanisms suggested for altered nerve function during pregnancy include changes in hormonal levels during pregnancy, which may decrease local anesthetic requirements, increased vascularity of the meninges, which could enhance drug transfer across the dura mater, hormonally induced alteration of the intercellular connective tissue matrix facilitating diffusion of LA across the nerve sheath, and other biochemical changes such as decreased buffering capacity that may sensitize nerves to LA. In the intact animal or human, mechanical

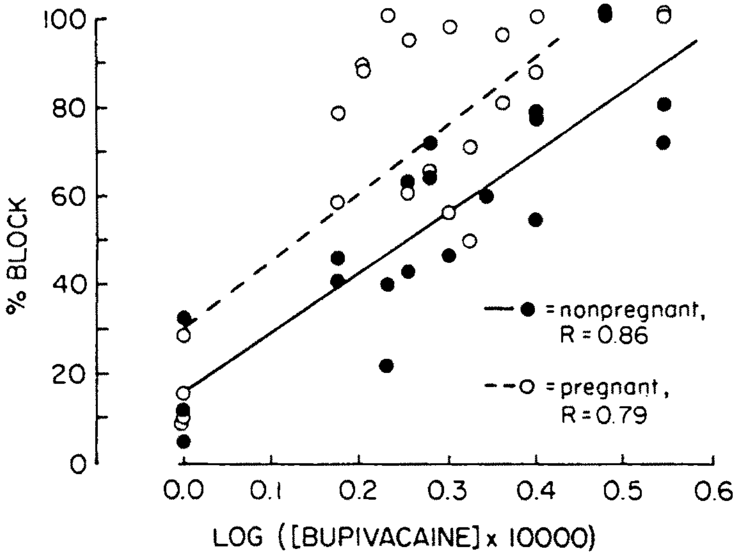


Figure 5. A fibers. Log-linear plot illustrating the effect of pregnancy on the reduction of peak-compound-action-potential amplitude of A fibers as a per cent of control after 30 minutes exposure to different concentrations of bupivacaine. The linear regression equation for pregnant subjects was per cent block = $30.5^a + 153 \log(\text{bupivacaine [M]} \times 10^4)$. The Cm = 0.134 mMol. In nonpregnant subjects, the linear regression equation was per cent block = $16.1^a + 136 \log(\text{bupivacaine [M]} \times 10^4)$. The Cm = 0.178 mMol; Cm is the concentration of bupivacaine corresponding to 50% block. [a]$P < 0.001$. (*From* Flanagan HL, Datta S, Lambert DH, et al: Effect of pregnancy on bupivacaine-induced conduction blockade in the isolated rabbit vagus nerve. Anesth Analg 66:123–126, 1987; with permission.)

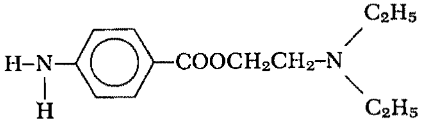
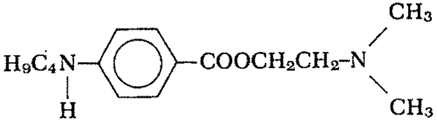
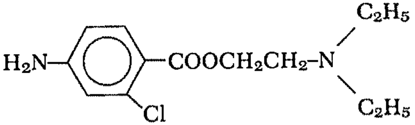
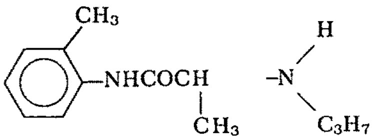
factors such as engorgement of the epidural veins from obstruction of the inferior vena cava by the pregnant uterus may cause increased spread of LA solutions and a decreased requirement for LA. Elevated progesterone levels reduce requirements for general anesthetics and may be involved in altered sensitivity to LA.[28, 66]

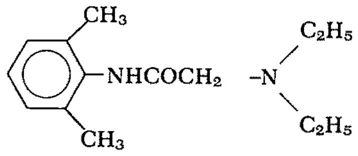
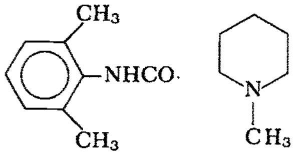
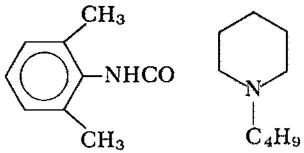
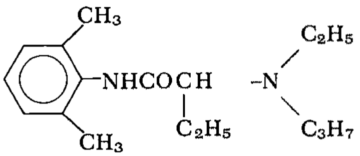
LOCAL ANESTHETIC CONSIDERATIONS

Structure-Activity Relationship

Clinically useful LA fall into either one of two categories based on their chemical structure. Amino esters (procaine, chloroprocaine, tetracaine) contain an ester linkage between the aromatic and hydrophilic portions of the molecule. Amino-amides (lidocaine, mepivacaine, prilocaine, bupivacaine, etidocaine) have an amide link between the aromatic and hydrophilic portions of their molecules (Table 2). The two groups of local anesthetics differ primarily in their allergenic potential and in their routes of metabolism. Para-aminobenzoic acid is one of the metabolites formed from the hydrolysis in plasma

Table 2. *Chemical Structure, Physicochemical Properties, and Pharmacologic Properties of Local Anaesthetic Agents*

AGENT	CHEMICAL CONFIGURATION			PHYSICOCHEMICAL PROPERTIES				PHARMACOLOGIC PROPERTIES		
	Aromatic Lipophilic	*Intermediate Chain*	*Amine Hydrophilic*	*Molecular Weight (Base)*	pK (25°C)	*Partition Coefficient*	*Protein Binding (%)*	*Onset*	*Relative Potency*	*Duration*
Esters										
Procaine				236	8.9	0.02	6	Slow	1	Short
Amethocaine				264	8.5	4.1	76	Slow	8	Long
Chloroprocaine				271	8.7	0.14	—	Fast	1	Short
Amides										
Prilocaine				220	7.9	0.9	55	Fast	2	Moderate

Lignocaine		234	7.9	2.9	64	Fast	2	Moderate
Mepivacaine		246	7.6	0.8	78	Fast	2	Moderate
Bupivacaine		288	8.1	27.5	96	Moderate	8	Long
Etidocaine		276	7.7	141	94	Fast	6	Long

From Covino BG: Pharmacology of local anaesthetic agents. Br J Anaesth 58:701–716, 1986; with permission.

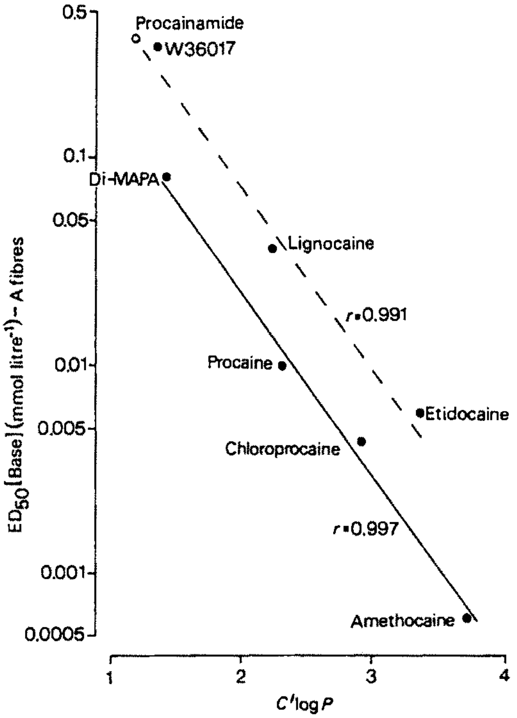


Figure 6. Relationship between ED_{50} [Base] and calculated lipid solubility. (*From* Wildsmith JAW, Gissen AJ, Takman B, et al: Differential nerve blockade: Esters vs. amides and the influence of pK_a. Br J Anaesth 59:379–384, 1987; with permission.)

of ester-type compounds and can produce allergic reactions. Amino-amides are metabolized in the hepatic microsomal system and do not produce para-aminobenzoic acid, hence allergic reactions are much less common. In addition, studies have suggested that the ester structure may have an inherently more potent action than the amino-amide structure at equivalent partition coefficient values (Fig. 6).[83]

With both the ester and the amide agents, the absolute local anesthetic potency correlates well with lipid solubility; however, an ester has an ED_{50} between one-half and one-sixth that of an amide of equal lipid solubility. Two possible explanations for the greater potency of the esters have been advanced.[24, 78] First, the amide bond is much "bulkier" and may physically restrict the access of the drug molecule to its binding site. Second, the 0-methyl groups present on the aromatic ring of lidocaine and its analogues may also interfere with binding to a receptor by causing the adjacent carbonyl oxygen to project away from the molecule.

Physicochemical Properties

Lipid Solubility. In general, potency increases as a function of lipid solubility until a partition coefficient of about 4 is reached. Further increases in lipid solubility do not appear to cause a further enhancement of anesthetic potency.[25, 26] Lipid solubility facilitates movement across cell membranes, all other factors being equal, and lipid solubility also enhances a drug's ability to cross membrane barriers such as the placenta and the blood-brain barrier. In addition, lipid solubility is related to local anesthetic toxicity.

pK_a. In solution, the LA exists both as uncharged molecules or base ($R \equiv N$) and as charged species or cations ($R \equiv NH^+$). The relative amounts of base and cation present will be determined by the pK_a of the specific compound and the pH of the solution. This relationship from the Henderson-Hasselbach equation, may be expressed as follows:

$$pK_a = pH - \log \frac{(R \equiv N)\ \text{base}}{(R \equiv H^+)\ \text{cation}}$$

The uncharged form of the molecule penetrates the nerve membrane, and the charged form combines with the receptor on the axoplasmic portion of the membrane to block sodium movement (Fig. 7). It follows from this that LA with pK_a values near pH 7.4 will have a greater proportion of uncharged molecules available when applied to a nerve and will have a shorter latency than those agents with high pK_a values. To a great extent, this is what is seen clinically. The short latency of chloroprocaine in spite of its pK_a of 8.9 is probably related in part to the high concentration (2%, 3%) of the drug used, depositing a relatively large number of uncharged molecules near the nerve although the number of charged molecules present is even higher.[26]

Protein Binding. Protein binding of LA is related to duration of action, is important in determining the potential for a toxic reaction by virtue of the amount of free versus bound drug in the blood, and may play some role in determining how much LA will reach the fetus. Most of the information regarding the protein binding of LA to their receptor, thought to be primarily protein, has been obtained from studies involving the binding of these drugs to plasma proteins. It is as-

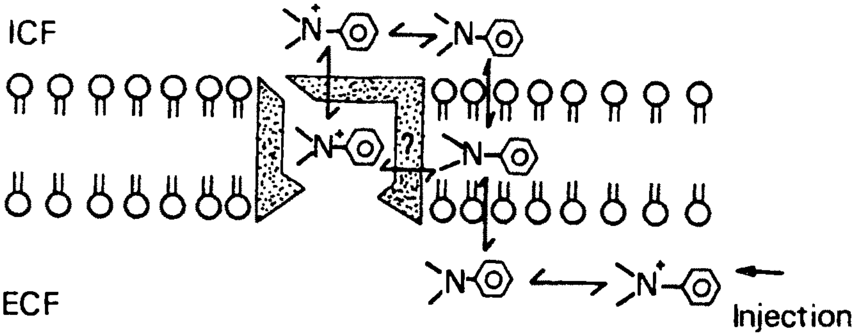


Figure 7. Access path of local anesthetic to sodium channel. (*From* Wildsmith JAW: Peripheral nerve and local anaesthetic drugs. Br J Anaesth 58:692–700, 1986; with permission.)

sumed that there is a relationship between the plasma protein binding of LA and the degree of binding to membrane proteins.[26]

Amide-type agents are bound mainly to alpha$_1$-acid glycoprotein (AAG), an acute phase protein; considerable variation in the plasma concentrations of this protein is a major source of variability in free drug fraction.[81] Albumin also binds LA but is a low affinity site. Pregnancy is one of a variety of conditions that may alter AAG levels, resulting in changes of free bupivacaine plasma concentration and thus the potential for toxic reactions.[29, 84] Total plasma bupivacaine concentrations may not give an accurate assessment of the risk of toxicity if accompanied by an elevation in AAG levels; the free fraction of plasma bupivacaine may actually be reduced under these circumstances.[84] The reverse would be true if AAG levels were decreased, as may occur during pregnancy.

Alexander[11] looked at the effects of hypercarbia on plasma lidocaine binding in humans. He saw decreased lidocaine protein binding while total plasma lidocaine remained constant; this would seem to indicate that the free fraction of lidocaine increased under conditions of respiratory acidosis and thus increased the risk of toxicity. This investigation complements the work done by Englesson[33] to examine the influence of acid-base changes on local anesthetic toxicity in the central nervous system (CNS).

The role of protein binding in limiting the amount of local anesthetic transferred to the fetus is complicated. Morishima measured blood and tissue LA levels in pregnant guinea pigs after maternal intravenous administration of lidocaine or etidocaine. Despite the higher percentage of protein binding of etidocaine compared with lidocaine, there were similar fetal tissue levels for both drugs, implying a similar degree of placental transfer.[60] Fetal:maternal plasma concentrations (F:M) of the highly protein-bound LA (bupivacaine, eti-

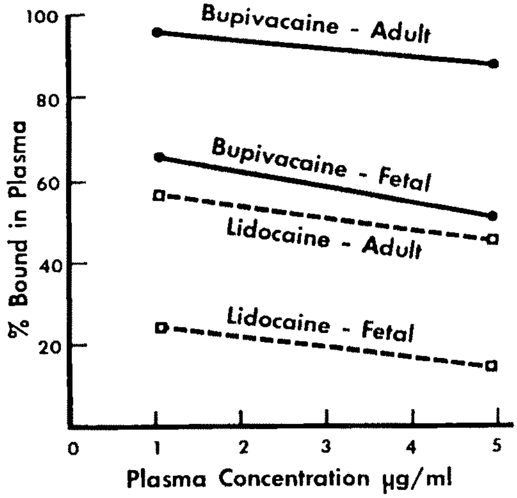


Figure 8. Protein binding of LAs. Placental transfer of LAs. Relative proportions of bupivacaine and lidocaine bound to plasma proteins in adult and fetal blood at concentrations between 1 and 5 µg per mL. (*From* Bromage PR: Epidural Analgesia. Philadelphia, Saunders, 1978; with permission. *Adapted from* Tucker GT, Boyes RN, Bridenbaugh PO: Anesthesiology 33:304–314, 1970; with permission.)

docaine) are low, ranging from 0.14 to 0.44, whereas less highly protein-bound drugs (lidocaine, mepivacaine) have F:M ratios of 0.5 to 0.7.[60] It has been suggested that the low F:M of bupivacaine may be due to extensive tissue uptake by the fetus rather than relatively slow placental transfer.[49] Carson,[18] however, was unable to demonstrate a progressive increase in fetal brain bupivacaine concentration over time using a rabbit model. Fetal brain:plasma ratios did exceed maternal ratios, but maximum fetal brain concentration of bupivacaine was 0.27 to 0.86 of maternal. Fetal AAG levels are lower than maternal levels and may account for the elevated brain:plasma ratios seen in the study (Fig. 8). Thus, there are implications for the development of toxicity in spite of low total fetal plasma bupivacaine concentrations, since free fraction of the drug may be elevated, particularly if there is any significant degree of fetal acidosis.

EPINEPHRINE

When large amounts of LA are used in nonobstetric settings, epinephrine is almost always incorporated in the local anesthetic injection, or in the test dose, in a concentration of 1:200,000 or 5 μg per mL. Epinephrine 1:300,000 (3.33 μg per mL) has been used clinically in obstetric anesthesia, as well as epinephrine 1:200,000, and seems to be equally effective in prolonging the duration of local anesthetic activity.[1, 6, 31]

Epinephrine serves several very important functions. First, it acts as a tracer to detect accidental intravascular injection; the usual test dose of 3 mL of local anesthetic with 15 μg of epinephrine will cause transient tachycardia and possibly hypertension in the non-β-blocked patient.[57] There will also be subjective feelings of nervousness, apprehension, and palpitation, all serving to warn of an intravascular injection. In addition, epinephrine tends to reduce the amount of LA reaching the circulation by decreasing uptake from the site of injection (Table 3). This is less true for lidocaine after subarachnoid than after epidural injection and is an inconsistent finding following bupivacaine epidural injection (Table 4).[1, 6, 30, 50] Differences in inherent vasodilator activity among the agents, as well as a complex interaction between site of injection, amount of fat present, and lipid solubility may explain some of the variability seen. Nevertheless, a reduction in the level of LA in the circulation reduces the risk of LA toxicity, all other factors being equal. Finally, epinephrine enhances LA activity, causing a greater degree of motor block and a longer duration of anesthetic action[15]; these effects are seen both with epidural lidocaine and bupivacaine.[1, 6, 31] These effects of epinephrine have been attributed to its localized vasoconstrictor activity, causing decreased removal of the drug from the site of injection and prolonged contact between drug and nerve. An additional contribution may be a direct analgesic effect via the α-adrenergic nociceptive system in the spinal cord dorsal horn.[85]

Table 3. *Plasma Concentrations of Lidocaine (μg/mL)*

	GROUP I *Lidocaine with Epinephrine (No. of samples)*	GROUP II *Lidocaine Alone (No. of samples)*
Maternal vein	1.32 ± 0.17 (9)	1.84 ± 0.18 (10)
Umbilical vein	0.56 ± 0.08* (9)	1.23 ± 0.26 (10)
Umbilical artery	0.61 ± 0.14 (7)	1.20 ± 0.28 (9)
Umbilical vein/ maternal vein ratio	0.42 ± 0.03* (9)	0.67 ± 0.08 (10)

Values are mean ± the standard error of the mean.

* $P < 0.05$ compared with group II patients as determined by Student's *t*-test.

From Abboud TK, David S, Costandi J, et al: Comparative maternal, fetal and neonatal effects of lidocaine versus lidocaine with epinephrine in the parturient. Anesth Analg 63:973–977, 1984; with permission.

There has been a hesitancy to use epinephrine with LAs in obstetrics.[7] There is concern that the accidental intravascular injection of 15 μg of epinephrine in a test dose will cause uterine artery vasoconstriction and decreased uterine blood flow (UBF); this does occur transiently and is of the magnitude and duration of that decrease in UBF occurring during a single uterine contraction (Fig. 9).[44] Larger amounts of epinephrine, from 50 to 100 μg, injected with LA

Table 4. *Plasma Concentrations of Bupivacaine (μg/mL)*

	GROUP I *Bupivacaine with Epinephrine (No. of samples)*	GROUP II *Bupivacaine Alone (No. of samples)*
Maternal vein		
10 minutes after injection	0.56 ± 0.07 (13)	0.43 ± 0.04 (16)
At time of delivery	0.57 ± 0.17 (13)	0.45 ± 0.12 (15)
Umbilical vein	0.19 ± 0.10 (13)	0.15 ± 0.04 (15)
Umbilical artery	0.17 ± 0.10 (12)	0.13 ± 0.04 (13)
Umbilical vein/maternal vein (at time of delivery)	0.27 ± 0.12 (13)	0.31 ± 0.08 (15)

Values are mean ± the standard error of the mean. No significant differences between groups by Student's *t*-test.

From Abboud TK, Sheikh-Ol-Eslan A, Yanagi T, et al: Safety and efficacy of epinephrine added to bupivacaine for lumbar epidural analgesia in obstetrics. Anesth Analg 64:585–591, 1985; with permission.

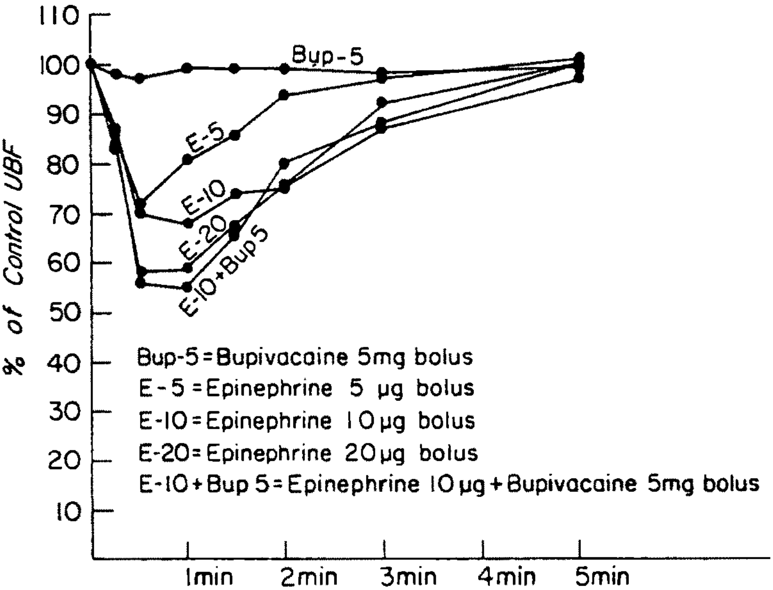


Figure 9. Alteration in uterine blood flow following intravenous injections of bupivacaine, epinephrine, and bupivacaine-epinephrine solutions. (*From* Hood DD, Dewan DM, Rose JC, et al: Maternal and fetal effects of intravenous epinephrine containing solutions in gravid ewes. Anesthesiology 59(Suppl):A393, 1983; with permission.)

into the epidural space have minimal effect on intervillous blood flow (IVBF) providing maternal blood pressure is maintained.[10, 46]

The hemodynamic effect of epinephrine absorbed from the epidural space is a β effect with vasodilation of vessels in skeletal muscle, a decrease in systemic vascular resistance, a decrease in mean arterial blood pressure, and an elevation in cardiac output. The fall in blood pressure can be prevented to a great extent by adequate volume expansion and left uterine displacement. The incidence of hypotension was not increased in patients receiving epidural bupivacaine with epinephrine for labor or cesarean section in studies by three investigators.[3, 31, 50]

Of equal concern has been the β effect of epinephrine on the uterus, which tends to decrease the force and frequency of uterine contractions and may prolong the second stage of labor. Eisenach's study showed no significant difference between the length of first or second stage of labor in patients receiving bupivacaine with epinephrine compared with those receiving plain bupivacaine.[31] There was no comment on the need to augment labors in either group.

To the extent that epinephrine decreases maternal blood levels of local anesthetic, an effect more pronounced with lidocaine than bupivacaine, there will be a reduced amount of drug transferred to the fetus and a reduction in the risk of maternal local anesthetic toxicity. This must be balanced with the potential risk of a transient decrease in IVBF should an intravascular injection occur. Each maternal/fetal pair has to be evaluated individually in this regard.

Moore has suggested that the use of epinephrine containing LA solutions facilitates resuscitation in the event of accidental intravascular injection with toxicity. The epinephrine may prevent profound LA-induced myocardial depression as has been reported with intravascular injections of bupivacaine.[9, 58] This has not been confirmed experimentally.[32]

pH ALTERATION

Dextran

To improve the efficiency of regional anesthesia in the clinical setting there have been attempts to increase the speed of onset and prolong the duration of action of LA. Loder[51] reported that dextran in a 50:50 mixture with lidocaine prolonged the duration of clinical nerve blocks from approximately 1.75 to 8.75 hours. Other studies have produced conflicting results, some showing prolongation, others not.[17, 74] Rosenblatt[74] proposed that dextran's major attribute is its alkalinity; thus, its mode of action as a LA adjuvant is analogous to that of sodium bicarbonate added to LA.[74] The inconsistent results obtained with dextran have been attributed to the different pHs of the various preparations used.

Sodium Bicarbonate ($NaHCO_3$)

Direct alkalinization of LA solutions with $NaHCO_3$ has been evaluated with regard to its effect on latency and duration of action.[37] Alkalinization favors the production of anesthesia through conversion of the ionized (water soluble) form to the nonionized (lipid soluble) form, since the LA are weak bases with pK_a values greater than 7.4. Experimentally, pH-adjusted lidocaine reduced the time to onset of nerve block in a linear fashion with incremental increases in pH.[65] A clinical study confirmed a shorter latency for alkalinized lidocaine (1 mEq $NaHCO_3$ added to 10 mL of anesthetic solution [pH 7.0]), in epidural anesthesia for cesarean section.[68] The study compared lidocaine plus epinephrine, 1:200,000, pH adjusted, with lidocaine plus epinephrine, commercial preparation (pH 4.5 to 5.0); in addition to differences in latency, there were significantly greater magnitudes and rates of decline in systolic blood pressure with alkalinized lidocaine plus epinephrine as compared with regular lidocaine plus epinephrine between 2 and 6 minutes after injection, which may be analogous to the hypotension that occurs during spinal anesthesia reflecting rapid onset of sympathetic blockade.

Addition of $NaHCO_3$ to bupivacaine has been evaluated; precipitation forms readily when $NaHCO_3$ is added to bupivacaine solutions and limits the degree to which the pH may be raised. Tackley[79] added

0.15 mL of 8.4% $NaHCO_3$ to 10 mL 0.5% bupivacaine with epinephrine 1:200,000 for a pH 6.3 and compared this with plain bupivacaine 0.5% pH 5.0 in epidural anesthesia for cesarean section. There was a more rapid onset of sensory and motor blockade in parturients receiving the alkalinized solution. Bavoux et al[14] increased the pH of 0.25% bupivacaine to 7.1 and 7.3 with sodium bicarbonate and noted no effect on latency but a linear increase in duration of analgesia with increasing pH in epidural analgesia for labor; there was no mention of precipitate formation. Similarly, McMorland,[54] using alkalinized bupivacaine in term parturients, found a statistically significant increase in duration of sensory analgesia. Alkalinized bupivacaine (pH 6.87) failed to shorten onset of action of spinal anesthesia in elderly patients for orthopedic surgery.[70] Finally, two recent studies have examined the effect of alkalinizing 2-chloroprocaine with sodium bicarbonate and looking at the quality and duration of subsequent epidural bupivacaine analgesia during labor and at the quality of post–cesarean-section analgesia with epidural morphine.[20, 45] Neither study demonstrated a difference between alkalinized and control preparations.

Carbonated Lidocaine

The pH of carbonated lidocaine, 6.5, is similar to that of plain lidocaine solution. Bromage et al[16] evaluated carbonated lidocaine in the clinical setting and found it superior to lidocaine hydrochloride in the quality of analgesia and the degree of motor block it produced. Subsequent clinical studies have differed in the ability to demonstrate unequivocal superiority of the carbonated preparation over the hydrochloride salt.[52, 62, 63, 67] Two of the most recent studies demonstrate that lidocaine hydrocarbonate produces a more rapid initial onset of sensory anesthesia as well as a more profound degree of motor blockade than lidocaine hydrochloride; there was no significant difference in duration of sensory and motor blockade between the two formulations.[63, 67] The effect of the carbonated preparation is more profound than can be explained solely on the basis of pH adjustment. Possible mechanisms by which carbon dioxide could potentiate the action of LA include (1) a direct depressant effect on the axon by carbon dioxide, (2) increased concentration of LA inside the nerve trunk (diffusion trapping), and (3) the conversion of LA to the active cation through the effect of CO_2 on pH at the site of action inside the nerve.[19] Interestingly, carbonation of bupivacaine does not bring about a significant improvement in clinical performance when compared with the hydrochloride salt.[15]

DRUG INTERACTIONS

H_2-Antagonists

Prophylactic administration of H_2-antagonists has been advocated to reduce the probability and sequelae of aspiration of gastric contents when pregnant patients require anesthesia. Cimetidine and ranitidine, the latter to a lesser extent, have been shown to reduce drug elimination by the liver through a reduction in liver blood flow and by inhibition of microsomal enzymes. Feeley et al[34, 35] found reduced clearance and increased toxicity of lidocaine by cimetidine, but failed to show a similar effect for ranitidine. In healthy male volunteers, two oral doses of cimetidine 400 mg given 10 hours apart caused a reduction in systemic clearance of bupivacaine. This was probably due to an effect of cimetidine on the metabolism of bupivacaine rather than any effect if present on hepatic blood flow because bupivacaine has a relatively low hepatic extraction ratio. Ranitidine 150 mg given on the same schedule had no significant effect on bupivacaine clearance.[64] Ranitidine 150 mg and cimetidine 400 mg in single oral doses given to term parturients prior to elective cesarean section with 0.5% bupivacaine epidural anesthesia were not associated with significant elevations of the plasma bupivacaine concentration, although levels were higher than in control patients.[36] In no case did the bupivacaine level exceed 0.8 to 0.9 μg per mL and the UV:MV ratio was around 0.3 in control and study patients.

FETAL EFFECTS OF LOCAL ANESTHETICS

Local anesthetics administered to the mother have direct effects on the fetus, determined by the actual amount of drug in fetal tissues. The transfer of drugs across the placenta occurs by passive diffusion and the rate of diffusion is proportional to the concentration gradient across the placenta and to the surface area available for diffusion. It is inversely proportional to the thickness of the membrane. Placental transfer is also determined by size of the drug molecule, the degree of ionization (which is related to pK_a and maternal and fetal pH), lipid solubility, and the degree of binding to plasma protein.[55] Other important factors include uteroplacental blood flow and placental drug binding. In addition, there may be indirect effects of LAs on the fetus through alteration of placental perfusion by means of changes in maternal cardiac output, peripheral resistance, oxygenation, and ventilation. Each maternal/fetal unit presents its own unique set of circumstances in which drug effect may be exhibited. Reduced placental perfusion may decrease the amount of drug transferred to the fetus, but the resulting acidosis in the fetus will cause a redistribution of the circulation with increased blood flow to brain and myocardium, increased ionization of the drug with "trapping" in the fetal circulation, reduced protein binding with an increase in the free fraction of circulating drug, and greater exposure of vital organs to potentially toxic amounts of local anesthetic.

Neurobehavioral Evaluation

Traditionally, the condition of the neonate after delivery has been evaluated by Apgar scores and acid-base status. In an attempt to gain

Table 5. *Elimination Rates of Local Anesthetics in the Adult and Neonate*

	SITE OF METABOLISM	ELIMINATION HALF-LIFE	
		Adult	*Neonate*
Bupivacaine	Liver	3.5 hours	<2 hours
Etidocaine	Liver	2.6 hours	—
Lidocaine	Liver	1.6 hours	3 hours
Mepivacaine	Liver	1.9 hours	9 hours
Chloroprocaine	Plasma	21 seconds	43 seconds

From Ralston DH, Shnider SM: The fetal and neonatal effects of regional anesthesia in obstetrics. Anesthesiology 48:34–64, 1978; with permission.

information on the more subtle and delayed effects possibly related to obstetric anesthesia and analgesia, neurobehavioral studies have been widely used over the past 15 years.[41, 43, 75, 80] Two of the tests used most commonly and reported in the anesthesia literature are the Early Neonatal Behavioral Scale (ENBS) introduced by Scanlon in 1974, and the Neurological and Adaptive Capacity Score (NACS) described by Amiel-Tison et al in 1982.[12, 75] Both evaluations are based on aspects of newborn motor performance and response to stimuli as recorded by trained observers, take 10 to 15 minutes to perform, and are done at standardized times following delivery, for example, 2 hours of age, 24 hours of age, 2 hours after feeding. However, when applied clinically, the studies have given considerable variation in results. Initial reports stated that lidocaine and mepivacaine epidural analgesia in the mother caused selective depression of motor performance in the neonate.[75, 80] However, this has not been confirmed for lidocaine or mepivacaine by subsequent studies.[1, 2, 5, 22, 23] Mepivacaine is rarely used now in obstetric anesthesia because of the awareness that the neonate is unable to metabolize the drug and must excrete it in the urine over time (Table 5). The literature also contains conflicting information regarding the effects of bupivacaine and chloroprocaine on neonatal neurobehavioral function.[47, 48] In general, the direct effects of local anesthetics on the neonate from maternal epidural anesthesia seem to be minimal. There are few statistically significant effects, and these are transient and so small that they probably lack clinical significance.[23, 80] Of far greater importance is maternal hypotension, with or without subsequent perinatal asphyxia. Hollman et al[43] found that the infants whose mothers experienced the greatest decrease in mean arterial pressure following epidural anesthesia showed poor motor organization for 2 days post-delivery. Thus, it would seem most important to preserve placental perfusion regardless of the anesthetic techniques or agent chosen.

The subjectivity of observers and difficulties in making quantitative measurements are drawbacks of neurobehavioral methods as is the lack of an appropriate drug-free control group. A further deficiency is the failure to consider everything happening in the perinatal period from which the neonate must recover.[23]

Quantitative EEG has been introduced as an objective and sensitive technique to detect subtle drug effects on the central nervous system (CNS) that may not be obtained by other techniques.[42] It provides very specific information. The neonatal EEG recorded during the first 2 hours after delivery confirms the depressant effect of thiopental used for general anesthesia cesarean section compared with 0.5% bupivacaine epidural anesthesia, thus agreeing with earlier studies using neurobehavioral techniques.[41, 43] Similarly, ephedrine causes a decrease in variability of the EEG pattern, which may be the result of a drug-induced decrease in total sleep time and an altered sleep pattern.[42] The clinical significance of these findings remains to be determined.

ADVERSE EFFECTS OF LOCAL ANESTHETICS

Bupivacaine

LAs entering the systemic circulation produce toxic effects primarily on the CNS but may also produce direct effects on the cardiovascular system (CVS) if present in high enough concentration. A rising blood level will consistently produce the following sequence of events: (1) numbness of the tongue and mouth, (2) lightheadedness, (3) tinnitus, (4) visual disturbance, (5) slurring of speech, (6) muscular twitching, (7) irrational conversation, (8) unconsciousness, (9) grand mal convulsion, (10) coma, and (11) apnea.[76] The sequence is similar for all local anesthetics that have been evaluated. Animal studies have shown that bupivacaine differs from lidocaine in two ways: (1) The ratio between the dose and blood level required for cardiovascular collapse and the dose and blood level required for production of CNS toxicity is significantly lower for bupivacaine as compared with lidocaine; and (2) bupivacaine in some animals is associated with the production of ventricular arrhythmias and ventricular fibrillation, which are not seen with lidocaine.[27, 61]

Studies in pregnant and nonpregnant sheep failed to show a clear difference in the cardiovascular collapse to CNS toxicity ratio for bupivacaine. Nevertheless, the blood level of bupivacaine at which cardiotoxicity occurred was lower in pregnant animals than in nonpregnant animals suggesting that the pregnant animal may be more sensitive to the potential cardiovascular toxic effects of bupivacaine.[27, 61] This was not related to a greater uptake of bupivacaine by the myocardium of the pregnant animals and suggests that the myocardium of the pregnant animal may be more sensitive to LA in the same way studies in isolated nerves suggest that the nerves of pregnant animals are more sensitive to the blocking effects of LAs.

Clarkson and Hondeghem[21] demonstrated a similar onset time for the block of sodium channels by high concentrations of lidocaine and bupivacaine. In high concentrations, lidocaine blocked sodium channels in a fast-in, fast-out manner. In low concentrations, bupivacaine blocked sodium channels in a slow-in, slow-out manner, whereas in high concentrations, the bupivacaine block was of the fast-in, slow-out type. Thus, the difference in in-vitro cardiotoxicity between LA agents seems to be related to their affinity for and duration of binding to the sodium channels. Bupivacaine may also block calcium channels to a significant degree. The electrophysiologic changes produced by bupivacaine suggest that re-entry phenomena may cause the severe ventricular arrhythmias.[56] Reiz and Nath[73] have summarized the studies on cardiotoxicity of LA.

Bupivacaine in high concentration (0.75%) is not recommended for use in obstetrics because of the profound myocardial depression and prolonged difficult resuscitations associated with accidental intravascular injections.

Chloroprocaine

Another constraint on the choice of an LA agent in the past decade has been related to the reports of prolonged neurologic deficit following the accidental subarachnoid injection of large amounts (> 400 mg) of chloroprocaine intended for epidural injection.[71, 72] Experimental investigations have tended to reaffirm the safety of the drug 2-chloroprocaine and have attributed the neurotoxicity to a combination of factors. The anti-oxidant sodium bisulfite in concentrations of 0.2% or greater in combination with the low pH (3.0) of the commercial solution probably is the source of the toxicity.[82] In addition, the large volumes of anesthetic solution used may overwhelm tissue-buffering capacity and furthermore, there is the potential for vascular compromise of spinal cord and nervous tissue particularly in pregnant patients who may have decreased intraspinal compliance because of engorged epidural veins.[39, 40] A bisulfite-free preparation of chloroprocaine has been evaluated clinically and found to provide satisfactory anesthesia for labor and delivery with no difference from the old bisulfite-containing formulation in regard to effects on uterine activity, progress of labor, fetal heart rate, maternal blood pressure, newborn Apgar scores, neonatal acid-base status, and the NACS.[4]

Prevention of Toxic Reactions

Most LA toxic reactions are preventable and those reactions that do occur can be successfully managed. However, the anesthesiologist performing the regional anesthetic technique must remain constantly alert to the possibility of an adverse reaction. Suggested guidelines to maximize the safety of an obstetric epidural block include selection of an agent that will provide adequate analgesia with minimal motor block, using the minimum amount of drug and lowest possible concentration to achieve the effect, careful performance of the epidural technique, careful and repeated aspiration, use of a test dose to indicate intravascular or subarachnoid injection, and use of a fractionated-dose technique to avoid the administration of a large mass of anesthetic as a single injection. Monitoring the parturient in terms of blood pressure and electrocardiogram while the block is performed, and advance preparation for the treatment of an adverse reaction should it occur are extremely important.[27, 59] Communication with the patient will enable rapid detection of the early subjective symptoms of a rising local anesthetic blood level.

Management of Toxic Reactions

The CNS is most sensitive to the action of LAs; however, toxic reactions involving the CVS tend to be more severe and more dangerous. With this in mind, it is important to determine the cause of the cardiovascular depression if present. Cardiac arrhythmias are probably best treated by electrical cardioversion; bretylium may facilitate this response.[73] Hypotension in the absence of arrhythmias is generally due to the negative inotropic effect of the LAs and the peripheral vasodilation they cause. Elevation of the legs and volume expansion are important therapeutic maneuvers. Resuscitation of the pregnant patient should always include left uterine displacement. Inotropes such as epinephrine, atropine, and calcium chloride have been successfully used in animal studies to reverse severe cardiovascular depression. Because hypoxia, hypercarbia, and acidosis occur with extreme rapidity following LA-induced convulsions and may potentiate cardiotoxic effects, it is important to maintain adequate ventilation. This may require the administration of a small dose of rapidly acting barbiturate or diazepam or succinylcholine to control convulsions.[27, 59, 73] Evacuation of the uterus has been required as part of the resuscitation on occasion.[53]

RECENT DEVELOPMENTS

Ropivacaine

Ropivacaine is an amino amide congener of mepivacaine and bupivacaine. It is a long-acting agent with a profile similar to that of bupivacaine, apart from some variations in duration of action depending on the site of administration. Ropivacaine appears distinctly longer acting than bupivacaine on infiltration, equally effective in peripheral blockade, and slightly shorter acting in central blockade. However, in epidural and spinal anesthesia 0.75% ropivacaine is equal in effect to 0.5% bupivacaine. Ropivacaine, in addition, may produce a high quality of sensory block in clinical use similar to that of bupivacaine. The drug is less toxic than bupivacaine but more toxic than lidocaine; in dog studies, it is less arrhythmogenic than bupivacaine and the margin of safety between the convulsant and the lethal dose is higher for ropivacaine than for bupivacaine.[8, 13] Furthermore, pregnant ewes are no more vulnerable to ropivacaine toxicity than nonpregnant ewes; doses of ropivacaine required to produce convulsions and circulatory collapse were significantly higher than those of bupivacaine.[69] Thus ropivacaine appears to be less cardiotoxic than bupivacaine in pregnant animals.

Narcotics

There is currently a great deal of interest in the use of epidural and intrathecal narcotics, by themselves and in combination with LAs. Such combinations have been used during labor, cesarean section, and for postoperative pain control. Spinal opioids are discussed at length in another article in this volume.

SUMMARY

LAs reversibly interrupt transmission of nerve impulses by inhibiting function of the sodium channel. Large myelinated rapidly conducting A fibers are most sensitive, and small unmyelinated slowly conducting C fibers, least sensitive to the block of transmission. Pregnancy may increase even further the A-fiber sensitivity to conduction block.

Of the clinically useful LAs, bupivacaine has become extremely popular in obstetric anesthesia because of its ability to create high quality analgesia with a minimum degree of motor block. The ability to cause this type of differential block is highly desirable and new LAs such as ropivacaine are evaluated with this in mind.

Epinephrine is a useful addition to LA solutions for purposes of detecting accidental intravascular injections and for improving the quality and duration of block, reducing the total amount of LA needed. However, there is a risk of temporary decrease in IVBF when accidental intravascular injection of epinephrine-containing solutions occurs.

Alkalinization of LA solutions with sodium bicarbonate enhances nerve block experimentally and may have a beneficial effect clinically. Similarly, carbonated lidocaine may have clinical advantages over lidocaine hydrochloride.

LA effects on the neonate have been evaluated by neurobehavioral testing. Inconsistent results and a failure to consider the multiplicity of factors surrounding parturition make it difficult to determine the clinical significance of these data.

Regarding the adverse effects of LAs, bupivacaine cardiotoxicity has been related to its fast-in, slow-out blocking of myocardial sodium channels. The pregnant animal may be more sensitive to this effect than the nonpregnant animal. Chloroprocaine has been reformulated without the anti-oxidant bisulfite, which along with the low pH of the earlier preparation is thought to have been responsible for the cases of neurotoxicity associated with accidental intrathecal injection of the drug.

Whenever large amounts of LA are used, there is the potential for the development of toxicity. The practitioner must strive to prevent

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LA toxicity but must remain alert to the possibility of its occurrence and be prepared to initiate effective treatment.

REFERENCES

1. Abboud TK, David S, Costandi J, et al: Comparative maternal, fetal and neonatal effects of lidocaine versus lidocaine with epinephrine in the parturient. Anesth Analg 63:973–979, 1984
2. Abboud TK, Kern S, Jacobs J: The neonatal neurobehavioral effects of mepivacaine for epidural anesthesia during labor. Reg Anaesth 11:143–146, 1986
3. Abboud TK, Kim KC, Noueihed R, et al: Epidural bupivacaine, chloroprocaine, or lidocaine for cesarean section—maternal and neonatal effects. Anesth Analg 62:914–919, 1983
4. Abboud TK, Mosaad P, Makar A, et al: Comparative maternal and neonatal effects of the new and the old formulations of 2-chloroprocaine. Reg Anaesth 13: 101–106, 1988
5. Abboud TK, Sarkis F, Blikian A, et al: Lack of adverse neonatal neurobehavioral effects of lidocaine. Anesth Analg 62:473–475, 1983
6. Abboud TK, Sheikh-Ol-Eslan A, Yanagi T, et al: Safety and efficacy of epinephrine added to bupivacaine for lumbar epidural analgesia in obstetrics. Anesth Analg 64:585–591, 1985
7. Abouleish E, Bourke D: Concerning the use and abuse of test doses for epidural anesthesia (letter). Anesthesiology 61:344–345, 1984
8. Ackerman B, Hellberg IB, Trossvick C: Primary evaluation of the local anaesthetic properties of the amino amide agent ropivacaine (LEA 103). Acta Anaesthesiol Scand 32:571–578, 1988
9. Albright GA: Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. Anesthesiology 51:285–287, 1979
10. Albright GA, Joupilla R, Hollman AI, et al: Epinephrine does not alter human intervillous blood flow during epidural anesthesia. Anesthesiology 54:131–135, 1981
11. Alexander CM, Berko RS, Gross JB, et al: The effect of changes in arterial CO_2 tension on plasma lidocaine concentration. Can Anaesth Soc J 33:343–345, 1987
12. Amiel-Tison C, Barrier G, Shnider SM, et al: A new neurologic and adaptive capacity scoring system for evaluating obstetric medications in full-term newborns. Anesthesiology 56:340–350, 1982
13. Arthur GR, Feldman HS, Norway SB: Acute IV toxicity of LEA-103, a new local anesthetic compared to lidocaine and bupivacaine in the awake dog. Anesthesiology 65(3A):A182, 1986
14. Bavoux E, Benhamou D, Clavier N, et al: Onset and duration of epidural analgesia with pH-adjusted bupivacaine. Is the change in pH the difference? Anesthesiology 69(3A):A393, 1988
15. Bromage PR: Epidural Analgesia. Philadelphia, Saunders, 1978, pp 144–145, 522–524
16. Bromage PR, Burfoot MF, Crowell DE, et al: Quality of epidural blockade III. Carbonated local anaesthetic solutions. Br J Anaesth 39:197–209, 1967
17. Buckley FP, Fink BR: Duration of action of nerve blocks produced by mixtures of local anesthetics and low molecular weight dextran: Studies in rat infraorbital nerve blocks. Anesth Analg 60:142–145, 1981
18. Carson RJ, Reynolds F: Maternal-fetal distribution of bupivacaine in the rabbit. Br J Anaesth 61:332–337, 1988
19. Catchlove RF: The influence of CO_2 and pH on local anesthetic action. J Pharmacol Exp Ther 181:298–309, 1972
20. Chestnut DH, Geiger MW, Bates JN, et al: The influence of pH-adjusted 2-chloroprocaine on the quality and duration of subsequent epidural bupivacaine analgesia during labor: A randomized, double-blind study. Anesthesiology 69(3A):A667, 1988

21. Clarkson CW, Hondeghem LM: Mechanism for bupivacaine depression of cardiac conduction: Fast block of sodium channels during the action potential with slow recovery from block during diastole. Anesthesiology 62:396–405, 1985
22. Cole CP, McMorland GH, Axelson JE: Comparison of neonatal neurobehavioral responses after lidocaine-HC1 and lidocaine hydrocarbonate epidural anaesthesia for caesarean section. Can Anaesth Soc J 31 (suppl):S68–69, 1984
23. Corke BC: Neonatal neurobehavior II: Current clinical status. Clin Anaesth 4: 219–227, 1986
24. Courtney KR, Strichartz GR: Structural elements which determine local anesthetic activity. In Strichartz GR (ed): Handbook of Experimental Pharmacology, vol 81. Heidelberg, Springer-Verlag, 1987
25. Covino BG: Clinical pharmacology of local anesthetic agents, *In* Cousins MJ, Bridenbaugh PO (eds): Neural Blockade, Pain Management, ed 2. Philadelphia, Lippincott, 1988
26. Covino BG: Pharmacology of local anaesthetic agents. Br J Anaesth 58:701–716, 1986
27. Covino BG: Toxicity of local anaesthetics in obstetrics III: Overview. Clin Anaesth 4:109–111, 1986
28. Datta S, Lambert DH, Gregus J, et al: Differential sensitivities of mammalian nerve fibers during pregnancy. Anesth Analg 62:1070–1072, 1983
29. Denson DD, Coyle DE, Thompson GA: Bupivacaine protein binding in the term parturient: Effect of lactic acidosis. Clin Pharmacol Ther 35:702–709, 1984
30. Denson DD, Bridenbaugh PO, Turner PA, et al: Neural blockade and pharmacokinetics following subarachnoid lidocaine in the rhesus monkey. I. Effects of epinephrine. Anesth Analg 61:746–750, 1982
31. Eisenach JC, Grice SC, Dewan DM: Epinephrine enhances analgesia produced by epidural bupivacaine during labor. Anesth Analg 66:447–451, 1987
32. Eisler EA, Shapiro DA, Shnider SM: The lethal dose of intravenous bupivacaine with and without epinephrine in rabbits. Anesth Analg 64:209, 1985
33. Englesson S: The influence of acid-base changes on central nervous system toxicity of local anaesthetic agents. Acta Anaesthesiol Scand 18:88–103, 1974
34. Feeley J, Guy E: Lack of effect of ranitidine on the disposition of lignocaine. Br J Clin Pharmacol 15:378–379, 1983
35. Feeley J, Wilkinson GR, McAllister CB, et al: Increased toxicity and reduced clearance of lidocaine by cimetidine. Ann Intern Med 96:592–594, 1982
36. Flynn RJ, Moore J, Collier PS, et al: Does pretreatment with cimetidine and ranitidine affect the disposition of bupivacaine? Br J Anaesth 62:87–91, 1989
37. Gissen AJ, Covino BG, Gregus J: Differential sensitivity of fast and slow fibers in mammalian nerve VI. Effect of pH on blocking action of local anesthetics (LA). Reg Anesth 11:132–138, 1986
38. Gissen AJ, Covino BG, Gregus J: Differential sensitivity of mammalian nerves to local anesthetic drugs. Anethesiology 53:467–474, 1980
39. Gissen AJ, Datta S, Lambert D: The chloroprocaine controversy I. A hypothesis to explain the neural complications of chloroprocaine epidural. Reg Anesth 9: 124–134, 1984
40. Gissen AJ, Datta S, Lambert D: The chloroprocaine controversy II. Is chloroprocaine neurotoxic? Reg Anesth 9:135–140, 1984
41. Hodgkinson R, Bhatt M, Kim SS, et al: Neonatal neurobehavioral tests following cesarean section under general and spinal anesthesia. Am J Obstet Gynecol 132:670–674, 1978
42. Hollman AI, Eskalinen P, Tolonen U, et al: Effects of anesthesia for cesarean section on the computerized EEG of the neonate. Eur J Anesth 2:39–51, 1985
43. Hollman AI, Joupilla R, Korvisto M, et al: Neurologic activity of infants following anesthesia for cesarean section. Anesthesiology 48:350–356, 1978
44. Hood DD, Dewan DM, James FM III: Maternal and fetal effects of epinephrine in gravid ewes. Anesthesiology 64:585–591, 1986
45. Hughes SC, Wright RG, Murphy D, et al: The effect of pH adjusting 3% 2-chloroprocaine on the quality of post-cesarean section analgesia with epidural morphine. Anesthesiology 69(3A):A689, 1988

46. Joupilla R, Joupilla P, Kuikka J, et al: Placental blood flow during caesarean section under lumbar extradural analgesia. Br J Anaesth 50:275–279, 1978
47. Kileff ME, James FM, Dewan DM, et al: Neonatal neurobehavioral responses after epidural anesthesia for cesarean section using lidocaine and bupivacaine. Anesth Analg 63:413–417, 1984
48. Kuhnert BR, Kennard MJ, Linn PL: Neonatal neurobehavior after epidural anesthesia for cesarean section: A comparison of bupivacaine and chloroprocaine. Anesth Analg 67:64–68, 1988
49. Kuhnert PM, Kuhnert BR, Stitts JM, et al: The use of a selected ion monitoring technique to study the disposition of bupivacaine in mother, fetus and neonate following epidural anesthesia for cesarean section. Anesthesiology 55:611–617, 1981
50. Laishley RS, Morgan BM, Reynolds F: Effect of adrenaline on extradural anaesthesia and plasma bupivacaine concentrations during caesarean section. Br J Anaesth 60:180–186, 1988
51. Loder RE: A local anesthetic solution with longer action. Lancet 2:346–347, 1960
52. Martin R, Lamarche Y, Tetreault L: Comparison of the clinical effectiveness of lidocaine hydrocarbonate and lidocaine hydrochloride with and without epinephrine in epidural anaesthesia. Can Anaesth Soc J 28:217–223, 1981
53. Marx GF: Cardiopulmonary resuscitation of late-pregnant women (letter). Anesthesiology 56:156, 1982
54. McMorland GH, Douglas MJ, Jeffrey WK, et al: Effects of pH-adjustment of bupivacaine on onset and duration of epidural analgesia in parturients. Can Anaesth Soc J 33:537–541, 1986
55. Mirkin BL: Perinatal pharmacology. Placental transfer, fetal localization, and neonatal disposition of drugs. Anesthesiology 43:156–170, 1975
56. Moller RA, Covino BG: Cardiac electrophysiologic effects of lidocaine and bupivacaine. Anesth Analg 67:107–114, 1988
57. Moore DC, Batra MS: The components of an effective test dose prior to epidural block. Anesthesiology 55:693–696, 1981
58. Moore DC, Scurlock JE: The possible role of epinephrine in prevention or correction of myocardial depression associated with bupivacaine. Anesth Analg 62:450–453, 1983
59. Moore DC: Toxicity of local anaesthetics in obstetrics IV: Management. Clin Anaesth 4:113–124, 1986
60. Morishima HO, Finster M, Pederson H, et al: Placental transfer and tissue distribution of etidocaine and lidocaine in guinea pigs. Abstracts, Annual Meeting, American Society of Anesthesiologists, Chicago, 1975, p 83
61. Morishima HO, Pederson H, Finster M, et al: Bupivacaine toxicity in pregnant and nonpregnant ewes. Anesthesiology 63:134–139, 1985
62. Morrison DH: A double-blind comparison of carbonated lidocaine and lidocaine hydrochloride in epidural anaesthesia. Can Anaesth Soc J 28:387–389, 1981
63. Nickel PM, Bromage PR, Sherrill DL: Comparison of hydrochloride and carbonated salts of lidocaine for epidural analgesia. Reg Anesth 11:62–67, 1986
64. Noble DW, Smith KJ, Dudas CR: Effects of H-2 antagonists on the elimination of bupivacaine. Br J Anaesth 59:735–737, 1987
65. Okamura RK, Reisner LS, Kalichman MW: Effects of pH-adjusted lidocaine solutions on the compound action potential in intact rat sciatic nerve. Anesthesiology 67(3A):A281, 1987
66. Palahnuik RJ, Shnider SM, Eger EI: Pregnancy decreases the requirements for inhaled anesthetic agents. Anesthesiology 41:82–83, 1974
67. Park WY, Hagins FM: Comparison of lidocaine hydrocarbonate with lidocaine hydrochloride for epidural anesthesia. Reg Anesth 11:128–131, 1986
68. Parnass SM, Curran MJ, Becker GL: Incidence of hypotension associated with epidural anesthesia using alkalinized and non-alkalinized lidocaine for cesarean section. Anesth Analg 66:1148–1150, 1987
69. Pederson H, Santos A, Morishima HO, et al: Systemic toxicity of ropivacaine in pregnant and nonpregnant ewes. Anesthesiology 69(3A):A344, 1988
70. Racle JP, Joudren L, Benkhadra A, et al: Effect of adding sodium bicarbonate to

bupivacaine for spinal anesthesia in elderly patients. Anesth Analg 67:570–573, 1988
71. Ravindran RS, Bond VK, Tasch M, et al: Prolonged neural blockade following regional analgesia with 2-chloroprocaine. Anesth Analg 59:446–451, 1980
72. Reisner LS, Hochman BN, Plumer MH: Persistent neurological deficit and adhesive arachnoiditis following intrathecal 2-chloroprocaine injection. Anesth Analg 59:452–454, 1980
73. Reiz S, Nath S: Cardiotoxicity of local anesthetic agents. Br J Anaesth 58:736–746, 1986
74. Rosenblatt RM, Fung DL: Mechanism of action for dextran prolonging regional anesthesia. Reg Anesth 5:3–5, 1980
75. Scanlon JW, Brown WV, Weiss JB, et al: Neurobehavioral responses of newborns after maternal epidural anesthesia. Anesthesiology 40:121–128, 1974
76. Scott DB: Toxic effects of local anaesthetic agents on the central nervous system. Br J Anaesth 58:732–735, 1986
77. Sevarino FB, Gilbertson LI, Gugino LD, et al: The effect of pregnancy on the nervous system response to sensory stimulation. Anesthesiology 69(3A):A695, 1988
78. Strichartz GR, Ritchie JM: The action of local anesthetics on ion channels of excitable tissues. *In* Strichartz GR (ed): Handbook of Experimental Pharmacology, vol. 81. Heidelberg, Springer-Verlag, 1987
79. Tackley RM, Coe AJ: Alkalinised bupivacaine and adrenaline for epidural caesarean section. Anaesthesia 43:1019–1021, 1988
80. Tronick E, Wise S, Heidelise A, et al: Regional obstetric anesthesia and newborn behavior: Effect over the first ten days of life. Pediatrics 58:94–100, 1976
81. Tucker GT: Pharmacokinetics of local anaesthetics. Br J Anaesth 58:717–731, 1986
82. Wang BC, Hillman DE, Spielholz NI, et al: Chronic neurologic deficits and nesacaine-CE. Anesth Analg 63:445–447, 1984
83. Wildsmith JAW, Gissen AJ, Takman B, et al: Differential nerve blockade: Esters vs. amides and the influence of pK_a. Br J Anaesth 59:379–384, 1987
84. Wulf H, Winckler K, Maier CH, et al: Pharmacokinetics and protein binding of bupivacaine in postoperative epidural analgesia. Acta Anaesthesiol Scand 32:530–534, 1988
85. Yaksh TL: Pharmacology of spinal adrenergic systems which modulate spinal nociceptive processing. Pharmacol Biochem Behav 22:845–858, 1985

Address reprint requests to

Esther C. Janowsky, MD
235 Huntington Drive
Chapel Hill, NC 27514

0889–8537/90 $0.00 + .20

Oxytocics, Tocolytics, and Prostaglandins

Stephanie A. Hughes, MD, [*]
and Brian L. Partridge, MD, DPhil [†]

This article reviews the physiologic effects of drugs administered in obstetrics to influence the tone of the uterus. These drugs include oxytocics, which stimulate uterine contraction, and tocolytics, which relax the uterus. The oxytocics reviewed include synthetic oxytocin, the ergot alkaloids, and those prostaglandins that influence uterine activity. Tocolytics covered include the β-sympathomimetics and magnesium sulfate. Each of these therapies has a unique side-effect profile that is a concern to the anesthesiologist. First, the physiology of the myometrium is briefly reviewed as a basis for understanding the actions of these drugs. Then, the pharmacology of each drug is reviewed and the possible side effects and complications are discussed.

PHYSIOLOGY OF THE MYOMETRIUM

The uterus is composed of smooth muscle that can generate multidirectional force. This allows a coordinated contraction around an irregularly shaped object, namely the fetus. The contractile unit is composed of myosin and actin proteins arranged in a unique geometry designed to contract in any direction. This differs from the rigid unidirectional contraction of skeletal, or striated, muscle.

Two contractile proteins, myosin and actin, form the contractile unit of smooth muscle and together generate the force of contraction. These two functional proteins rest in a matrix of structural proteins. The myosin filament has two sections: a linear portion called the tail,

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[*] Chief Resident, Department of Anesthesiology, University of California, San Diego Medical Center, San Diego, California

[†] Assistant Professor of Anesthesiology, University of California, San Diego Medical Center and San Diego VA Medical Center, San Diego, California

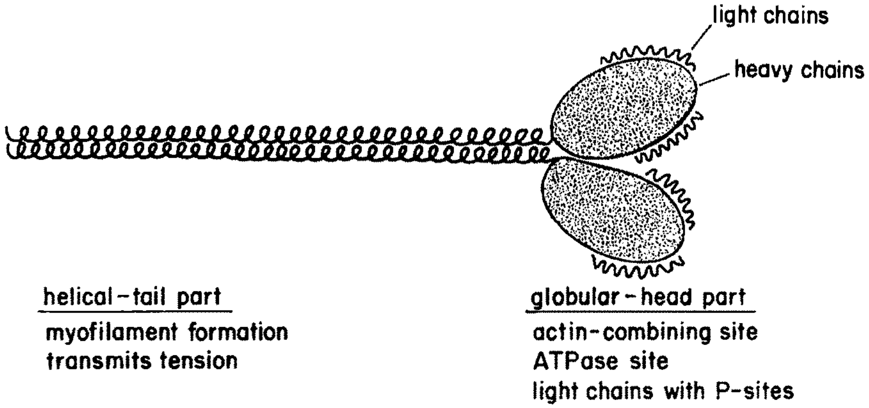

Figure 1. Schematic structure of myosin in smooth muscle. (*Adapted from* Huszar G: Physiology of the myometrium. *In* Creasy RK, Resnik R (eds): Maternal-Fetal Medicine. Philadelphia, Saunders, 1984; with permission.)

and a globular section at one end referred to as the head. The head contains three important sites: (1) the actin-combining site where myosin and actin interact, (2) an ATP-ase site for energy, and (3) the light chains that regulate the interaction of myosin and actin (Fig. 1). Myosin in smooth muscle is arranged at intervals next to the protein actin. The globular portion of myosin, "the head," serves as a hook with which myosin is pulled along the actin filament. The coordinated sliding motion of multiple myosin and actin units leads to muscle fiber shortening and uterine contraction. This interaction is energy dependent and intricately regulated by a chain of events that supplies energy via ATP to stimulate the movement of myosin along actin.[33]

The myosin light chains on the head of the myosin filament ultimately serve to regulate this interaction. The regulation pathway leading to uterine contraction begins with an increase in myoplasmic calcium concentration, which activates myosin light chain kinase. This kinase phosphorylates myosin light chains. Following phosphorylation, the light chains facilitate the interaction of the actin-combining site of myosin with actin. The myosin filament then slides along the actin filament generating muscle fiber shortening.

This series of events is regulated by two enzymes: (1) myosin light chain kinase, which transforms the light chains to the active form, and (2) myosin light chain phosphatase, which dephosphorylates the myosin light chain filament to an inactive state.

Activity of myosin light chain kinase is further influenced by three factors, two of which facilitate activity and one which is inhibitory. The first positive influence is myoplasmic calcium concentration. Second, a regulating enzyme, calmodulin, must be present for activity. Third, a cyclic-adenosine-monophosphate (cAMP)–dependent phosphorylation of the kinase is inhibitory; consequently, an increase in myometrial cAMP levels negatively influences the activity of myosin light chain kinase. An increase in cAMP also stimulates sequestration of calcium, further inhibiting contraction. Therefore, conditions that favor an increase in uterine tone are an increase in myoplasmic calcium and a relatively low concentration of cAMP.

The oxytocic and tocolytic medications described in this article act by affecting the intracellular environment of the myometrium to augment or decrease contraction frequency and strength. Oxytocin increases uterine tone by inhibiting the intracellular sequestration of calcium. Prostaglandins are also thought to positively influence the frequency and strength of uterine contractions by altering calcium movement. The β-adrenergics used for tocolysis and uterine relaxation cause an increase in the activity of adenylate cyclase and thus the synthesis of more cAMP. This increase in cAMP stimulates phosphorylation and inhibition of mysosin light chain kinase. The β-adrenergic–mediated increase in intracellular cAMP also promotes calcium sequestration in the sarcoplasmic reticulum, further inhibiting the contractile pathway.

OXYTOCICS

In current obstetric practice, oxytocics are used to increase uterine contractility in a variety of settings. They may be employed to "ripen" the cervix and initiate labor in the antepartum patient, to augment labor that is inadequate, to stimulate abortion, or to combat uterine atony and resultant hemorrhage postpartum. Three drug classes serve to increase the frequency and strength of uterine contractions. These three are synthetic oxytocin, the ergot alkaloids, and select prostaglandins.

Oxytocin

Oxytocin, a peptide of nine amino acids originally extracted from the pituitary gland, is available as a synthetic hormone with an amino acid sequence identical to biologic oxytocin. Pituitary extracts of oxytocin that were formally available were inevitably contaminated with vasopressin, another posterior pituitary hormone. Synthetic oxytocin is now manufactured avoiding contamination. Uterine sensitivity to, and the number of uterine receptors for, oxytocin increase near term. This hormone appears to influence the uterus by increasing myoplasmic calcium concentration leading to an increase in myosin-actin interaction resulting in increased strength and frequency of contractions.

Administration methods for oxytocin vary according to the therapeutic indications. For induction or augmentation of labor, a slow continuous infusion of oxytocin at a rate of 10 to 40 mU per minute may be used. Postpartum, an infusion of 10 to 20 U oxytocin in 1 L of intravenous (IV) fluid at a rate of 200 mL per hour or intramuscular injection of 10 to 20 U are recommended administration modes.[52] The plasma half-life is 12 to 17 minutes.[3] Onset of uterine response to IV

Table 1. *Side Effects and Complications of Oxytocics*

DRUG	SIDE EFFECTS AND COMPLICATIONS
Oxytocin	Hypotension: decreased SVR, MAP; resultant increased HR, CO Anti-diuretic activity: hyponatremia, oliguria, water intoxication Uterine hypertonicity: decreased uterine blood flow, uterine rupture
Ergonovine and methylergonovine	Arterial and venous vasoconstriction: hypertension, increased CVP and SVR, pulmonary edema, seizures, cerebral edema, intracerebral hemorrhage, cardiac arrest Coronary vasospasm: myocardial ischemia
Prostaglandins	Nausea, vomiting, diarrhea, restlessness, tachypnea, tachycardia
PGE_2	Decreased SVR, MAP; increased CO, HR, unchanged PVR
$PGF_{2\alpha}$	Increased MAP, HR, CO, PRV; bronchoconstriction

administration of oxytocin occurs almost immediately and lasts approximately 1 hour.[52] With intramuscular (IM) administration, the onset is within 2 to 5 minutes and the duration of effect is 1 to 3 hours.[52]

Although commercial preparations of oxytocin are no longer contaminated with vasopressin, oxytocin does have direct actions and inherent properties other than its uterotonic effects, which must be kept in mind when administering it. The principal side effects include possible hypotension and free water overload (Table 1).

Oxytocin is a direct vasodilator. Weis et al[58] showed that administration of oxytocin in an IV bolus of 0.1 U per kg leads to a 30% drop in mean arterial pressure (MAP), a 50% decrease in systemic vascular resistance (SVR), and a compensatory tachycardia and increase in stroke volume augmenting cardiac output. The inotropic and chronotropic actions are reflex sympathetic responses to the drop in peripheral vascular resistance and are seen within 30 seconds after the IV bolus.[40] Usually, the hypotensive effects are transient and last approximately 5 minutes. Because of the potential for hypotension with bolus dosing of oxytocin, an IV infusion at 40 to 80 mU per minute or IM injection are recommended for treatment of postpartum uterine atony.

Oxytocin has intrinsic antidiuretic activity. The structural similarity of oxytocin to vasopressin—differing by only two amino acids—probably explains this action. ADH-like activity leads to an increase in water resorption in the distal convoluted tubule of the kidney and a drop in urine output following oxytocin administration.[1, 47] Patients receiving large doses or prolonged infusion of oxytocin should be observed for possible water intoxication. Hyponatremic, hyposmotic states have been demonstrated after prolonged infusions at rates up to 40 mU per minute oxytocin in large volumes of electrolyte-free fluids.[19] The fetus also experiences this state of relative water overload and Schwartz and Jones[48] reported hyponatremic seizures in both the mother and newborn following a maternal infusion of 6.5 L D_5W and 36 U of oxytocin.

Ergot Alkaloids

The toxic and many of the therapeutic effects of the ergot derivatives have been known for centuries. Ergot, actually a complex of multiple biologically active amines, is produced by a fungus (*Claviceps purpurea*) that may infest grain crops, particularly rye. Epidemics resulting from ingestion of the infected grain were known in the Middle Ages. Victims experienced the symptoms of severe vasoconstriction that sometimes resulted in dry gangrene of the extremities. In addition to the vasoactive properties of ergot derivatives, the potent uterine stimulating properties of ergot were appreciated and employed therapeutically in obstetric practice by the early 1800s and probably earlier.[45]

The complex substance ergot has since been studied extensively and many of its active substances identified. Two derivatives are used in current obstetric practice, ergonovine and methylergonovine. Ergot alkaloids are restricted to use in the postpartum period to increase uterine tone and halt bleeding because their uterine-stimulating properties are so great that the possibility of tetanic contractions or an increase in resting tone may risk fetal well-being. The uterotonic effects are the result of direct α-adrenergic receptor stimulation.[36]

Ergonovine (Ergotrate maleate) and methylergonovine (Methergine) are available for both injection (0.2 mg per mL) and oral administration as 0.2-mg tablets. Common dosing regimens for postpartum uterine atony are 0.2 mg given either IM or orally. Therapeutic response can be seen within 3 to 5 minutes after IM injection and within 10 minutes of oral administration.[45] The β-elimination half-life of methylergonovine is between 32 to 115 minutes.[36] Elimination is via hepatic metabolism.

Although ergonovine and its semisynthetic derivative methylergonovine are less toxic than some other ergot derivatives, they are not without significant side effects, most notably vasoconstriction. The central nervous system (CNS) as well as the cardiovascular system may manifest symptoms resulting from generalized vasoconstriction. Ergot alkaloids constrict both the arterial and venous sides of the circulation.[34] This property can lead to hypertension and an augmentation of central circulating fluid volume. Brooke and Robinson[7] observed that 0.25 mg of ergonovine IV led to a decrease of forearm venous compliance of 41% associated with an increase of MAP and central venous pressure (CVP). In select patients, the hypertension may be life threatening.

Complications arising from this widespread vasoconstriction with resultant increases in SVR, MAP, and CVP have included pulmonary edema, heart failure, retinal detachment, seizures, cerebral edema, and intracerebral hemorrhage.[2, 8, 10, 34, 46] Abouleish[2] reported severe prolonged postpartum hypertension in an otherwise healthy parturient that resulted in cerebral edema and seizures. Following 0.2 mg of methylergonovine IV, this patient demonstrated a remarkable postpartum blood pressure increase to 200/130 from an antepartum blood pressure of 110/65. The hypertension was accompanied by headache and subsequent seizures. Browning[8] also reported similar hypertensive crises in four patients, one of which resulted in a seizure and one in cardiac arrest.

The marked hypertension following the administration of parenteral methylergonovine or ergonovine can last for several hours.[34] A rise in blood pressure occurs in 20 to 50% of patients given one of these ergot preparations.[52] The percentage of hypertensive events and the absolute rise in blood pressure increases with concurrent or prior administration of vasopressors. This synergism is seen with ergot administered even several hours after vasopressor administration. A large study of parturients by Casady et al[10] demonstrated that almost 5% of patients who received methoxamine and subsequent ergotamines had a rise in systolic blood pressure to greater than 140 mm Hg and two-thirds of these developed a diastolic pressure of 100 mm Hg or greater. Ergots appear to be partial agonists at adrenergic, tryptaminergic, and dopaminergic receptor sites. This agonism may explain the synergistic pressor response possible when ergots are given to the patient who has received vasopressors. However, because this interaction is more than additive, simple agonism at the same sites cannot completely explain the phenomenon.[45]

In addition to the stresses it places on the maternal heart from an acute increase in SVR, methylergonovine may further stress the myocardium by stimulating coronary vasospasm.[9] In fact, ergotamine has been used in the controlled setting of the coronary catheterization laboratory as a challenge test to provoke coronary spasm.[23] Taylor and Cohen[54] published a case report of morbidity associated with coronary vasospasm and ergots in a pregnant patient that resulted in a large anterior wall myocardial infarction. The propensity for coronary vasospasm may be increased in patients with other vasospastic diseases such as migraine headaches.[39] Other side effects associated with ergotamines include nausea and vomiting in approximately 10 to 20% of patients as a result of direct stimulation of the CNS emetic centers.[45]

Because of the side-effect profile, ergotamines are relatively contraindicated in the obstetric patient with a history of hypertension, preeclampsia, eclampsia, cardiac disease, peripheral vascular disease, prior vasopressor administration, and possibly patients with such vasospastic disorders as Raynaud's phenomenon. Recognition of anginal symptoms and proper evaluation of the patient with suspected coronary vasospasm is mandatory. Therapy with nitroglycerin should be instituted when the diagnosis of coronary vasospasm is made.[9, 30]

Prostaglandins

Select prostaglandins are potent uterine stimulants. Prostaglandins of both the E and F classes are employed in obstetrics. Their actions on the myometrium appear to be mediated by alteration of intracellular calcium flux. Prostaglandin use in obstetrics ranges from vaginal suppositories and intra-amniotic instillation for second trimester abortions to effective therapy for postpartum hemorrhage resulting from uterine atony. Prostaglandin gels are also employed to facilitate ripening of the cervix as part of the induction of labor. The commercial prostaglandins for use in obstetrics are dinoprostone (PGE_2), dinoprost tromethamine ($PGF_{2\alpha}$), and carboprost tromethamine (15-methyl $PGF_{2\alpha}$, Prostin/15M). Dinoprost tromethamine ($PGF_{2\alpha}$) is currently unavailable from the manufacturer.

Prostaglandin E_2 vaginal suppositories are employed in the management of missed abortions and as mid-trimester abortifacients. $PGF_{2\alpha}$ may be instilled intra-amniotically for pregnancy termination. $PGF_{2\alpha}$ or the methylated analog 15-methyl $PGF_{2\alpha}$ are administered IM or intramyometrially to treat postpartum hemorrhage. Usual IM dosage for treatment of postpartum atony is 1 mg of $PGF_{2\alpha}$ or 250 μg of 15-methyl $PGF_{2\alpha}$. This dose may be repeated in 15 minutes.

The effects of these prostaglandins are not limited to the uterus. They each influence the cardiovascular, respiratory, gastrointestinal, and central nervous systems to varying degrees. Noted among their side effects are nausea, vomiting, diarrhea, restlessness, tachypnea, tachycardia, bronchoconstriction, and changes in pulmonary and systemic vascular tone.

Vaginal suppositories of prostaglandin E_2 in doses from 5 to 20 mg every 3 hours are used to induce termination of pregnancy. The common side effects of this therapy include nausea, vomiting, diarrhea, tachypnea, pyrexia, moderate hypotension, and tachycardia. The gastrointestinal side effects are the result of intestinal smooth muscle stimulation. Cardiovascular side effects are dose dependent and include a moderate reduction in systemic vascular resistance and blood pressure and an increase in cardiac output and heart rate. This increase in cardiac output and heart rate appears to be a reflex-mediated sympathetic response to the reduction in SVR.[20, 50] Secher et al[50] noted a 36% increase in cardiac output, a 31% decrease in blood pressure, and a 33% decrease in SVR in patients receiving a PGE_2 infusion. Willis et al[59] noted an even greater cardiac output increase, 65%, in patients receiving PGE_2 vaginal suppositories for mid-trimester abortion.

Tachypnea is common with PGE_2 therapy. Animal data have suggested that PGE_2 may increase pulmonary vascular resistance (PVR); however, Secher et al noted no change in pulmonary vascular tone in patients receiving IV infusions of PGE_2. Eklund and Carlson's[20] study of eight male patients receiving PGE_1 or PGE_2 noted no change in pulmonary artery pressure despite an increase in cardiac output, implying a decrease in PVR.

In addition to the cardiovascular and respiratory side effects of PGE_2, hyperpyrexia is often seen. Up to 40% of patients will manifest a pyrexic response.[43] In fact, the clinical picture of high fever, hypotension, tachycardia, and tachypnea mirrors the presentation of endotoxin-mediated shock. Phelan et al[43] described two cases in 1978 and Hughes and Hughes[32] reported a case in 1989 of dramatic fever and cardiovascular symptoms in which the diagnosis of endotoxemic shock was entertained during PGE_2 therapy. In each case, the patients proved not to be septic, and the symptoms subsided after discontinuation of PGE_2. Because most patients receiving PGE_2 will have some degree of gastrointestinal symptoms and pyrexia, antipyretics, anti-emetics, and anti-diarrheals are routinely ordered at some institutions.

The majority of physiologic effects of the prostaglandins of the F series are similar to the E series; however, the hemodynamic consequences are different. Both series stimulate uterine contraction and cervical dilation, though with $PGF_{2\alpha}$ the effects on uterine tone predominate over cervical dilation.[32] Prostaglandin $F_{2\alpha}$ increases intestinal motility via smooth muscle stimulation so that nausea, vomiting, and diarrhea are common. Also similar to PGE_2, an elevation of patient temperature may be seen. $PGF_{2\alpha}$ stimulates bronchial smooth muscle leading to bronchoconstriction.[51] Oxygenation may decrease because of a redistribution, and increase in mismatch, of ventilation and perfusion.[50]

Hemodynamic disturbances associated with $PGF_{2\alpha}$ include an increase in blood pressure, heart rate, and cardiac output. Pulmonary vascular tone increases. During infusion of $PGF_{2\alpha}$ 300 μg per minute in five anesthetized patients, Secher et al measured an increase of femoral artery pressure of 40% concomitant with a 25% increase in cardiac output, and an 11% decrease in systemic vascular resistance. These changes were accompanied by a significant increase in calculated PVR (125%). Eklund gave 15-methyl $PGF_{2\alpha}$ at 0.07 μg per kg per minute and demonstrated an increase in cardiac output, heart rate, and blood pressure at 30%, 12%, and 19%, respectively. Increases in right heart pressures and pulmonary artery pressure were also noted.

The magnitude of cardiopulmonary changes with $PGF_{2\alpha}$ can be life threatening. Cates et al[11] reviewed six abortion-related deaths associated with the use of $PGF_{2\alpha}$ intra-amniotically. Four had intercurrent illness. One chronic alcoholic with pontine myelinolysis died from aspiration of hematemesis; the emetic effects of the prostaglandin may have been contributory. The second patient had chronic hypertension with superimposed preeclampsia. After receiving $PGF_{2\alpha}$ she sustained a hypertensive crisis and died of an intracranial hemorrhage. The four other patients died of causes seemingly unrelated to the prostaglandin: amniotic fluid embolism, sedative overdose, microscopic pulmonary emboli with cor pulmonale, and sepsis complicated by hemorrhagic-hemolytic syndrome. Subsequent to that report, Cates and Jordaan[12] published two cases of unexplained cardiovascular collapse following instillation of $PGF_{2\alpha}$. In 1988, Partridge et al[41] reported life-threatening hypertension, bronchospasm, and severe peripheral vasoconstriction in a patient who received intra-amniotic $PGF_{2\alpha}$. Hypertension alternated with hypotension and continued for 2 hours until artificial rupture of the amniotic membranes and release of the remaining $PGF_{2\alpha}$. The clinical picture was that of repeated intravascular boluses of prostaglandin with each uterine contraction.

TOCOLYTICS

In the United States in 1980, the incidence of preterm births, defined as any birth that occurs before 37 completed weeks from the first day of the last menstrual cycle, was 8.9%.[15, 56] Preterm labor and delivery are a significant cause of perinatal morbidity and mortality. Tocolytics are used to stop premature uterine contractions and inhibit the return of preterm labor. Two classes of drugs are commonly employed as tocolytics: The β-sympathomimetics and magnesium sulfate. Both work at the level of the myometrium to decrease contractility. Ethanol has been used as a tocolytic; however, it has generally been superceded by the other agents. Calcium channel antagonists and prostaglandin synthesis inhibitors have also been investigated as possible therapies for preterm labor.

β-Sympathomimetics

β-Adrenergic agents are the most widely used tocolytics. The most common include ritodrine, terbutaline, isoxsuprine, fenoterol, and salbutamol. β_2 Sympathomimetic stimulation of the uterus causes relaxation. Stimulation of the β_2-receptor at the myometrial cell leads to an increase in cAMP with subsequent phosphorylation and inhibition of myosin light chain kinase, thus blocking the contractile interaction of myosin and actin. Contraction is also inhibited by a reduction in myoplasmic free calcium that occurs with an increase in cAMP.

Though the beta-adrenergic agonists used as tocolytics are selected for their predominance of β_2-over β_1-activity, they all have side effects from stimulation of both receptors. β_2 effects include a decrease in smooth muscle tone of the uterus, vasculature, and bronchioles. Renin levels increase and urinary output decreases. Glycogenolysis is stimulated as well as an increase in insulin release. β_1-adrenergic stimulation causes an increase in heart rate and stroke volume, lipolysis, and transport of potassium into cells. Bowel motility is decreased.[15] Most of these agents are excreted by the kidney. After IV infusion of ritodrine there is an initial distribution half-life of 5 to 10 minutes, a secondary half-life of 1.5 to 2.5 hours, and a prolonged third phase. After oral ritodrine there is an initial half-life of 1 to 2 hours with a subsequent 10 to 12-hour half-life. Complications of β-sympathomimetic therapy include hypotension, myocardial ischemia, pulmonary edema, and alterations in glucose and electrolyte balance (Table 2).

These β-adrenergic agonists are inotropic and chronotropic stimulants of the myocardium.[5, 31] Bieniarz et al[5] demonstrated the net result of this stimulation to be an increase in cardiac output over and above the already augmented cardiac output of pregnancy. Using a dye dilution technique for measurement of the cardiac output in five

Table 2. *Side Effects and Complications of Tocolytics*

DRUG	SIDE EFFECTS AND COMPLICATIONS
Beta-sympathomimetics	Decreased smooth muscle tone: uterus, vasculature, bronchioles Increased renin: decreased urine output Glycogenolysis, insulin release: increased serum glucose, decreased potassium Increased heart rate, stroke volume Myocardial ischemia Pulmonary edema
Magnesium sulfate	Central nervous system depression, respiratory failure, cardiac depression, pulmonary edema, flushing, headache, nausea, decreased ionized calcium, potentiation of muscle relaxants

patients in premature labor who received ritodrine infusion titrated to uterine relaxation, a peak increase of cardiac output of 56% was achieved. This was accompanied by a decrease in peripheral vascular resistance and a significantly widened pulse pressure. Systolic blood pressure increased 12%, while diastolic blood pressure decreased by 10%, maintaining the calculated mean arterial pressure essentially unchanged. The maternal heart rate significantly increased by 16% after 20 minutes of infusion. Stroke volume also increased. Studies of terbutaline provide similar results.[48, 56] These studies demonstrate the cardiovascular consequences of administering a β-mimetic agent for uterine relaxation.

In addition to the effects described previously, severe cardiovascular side effects have been reported. Myocardial ischemia is a potential complication. Several authors have documented electrocardiographic changes suggestive of ischemia during ritodrine or terbutaline infusion.[35, 38, 55, 60] ST-segment depression and T-wave inversion were not always accompanied by angina. Generally, the electrocardiogram returned to baseline after discontinuation of the β-sympathomimetic. Because of these case reports of potential myocardial ischemia associated with β-mimetic therapy, a baseline electrocardiogram prior to therapy has been recommended.[26] Following serial electrocardiograms in patients receiving β-adrenergic infusion is reasonable; however, the frequency of electrocardiogram changes in asymptomatic patients is quite high when viewed on a prospective basis. Hendricks et al[29] documented that 76% of 112 patients receiving ritodrine tocolysis had either ST-segment changes, T-wave changes, or both. Reassuringly, only two of the patients had significant consequences: both experienced severe angina, and one of the two developed pulmonary edema attributed to volume overload. Thus, electrocardiographic changes may be a frequent occurrence without symptoms or sequelae. The value of anti-anginal therapy and the question of whether or not to discontinue tocolytic therapy when these changes are seen remains unclear.

The most serious complication of β-adrenergic tocolytic therapy is pulmonary edema. The incidence of pulmonary edema in β-mimetic-treated patients may be as high as 5%.[35] Women with twin gestations appear to be at particular risk, probably because of the patient's already augmented vascular volume and cardiac output. It is not clear what mechanism explains pulmonary edema in this setting. Possibilities include cardiac decompensation, volume overload, and a change in the regulation of the delicate pulmonary intravascular-to-extravascular fluid balance. In patients studied prospectively, improvement in cardiac function with increased stroke volume, ejection fraction, fractional shortening, and unchanged left ventrical dimensions all argue against cardiac decompensation.[31, 56] Benedetti et al[4] reported normal pressures and pulmonary vascular resistance shown with a pulmonary artery catheter placed in a patient after the development of pulmonary edema, suggesting that the etiology is not cardiogenic. However, no reports of invasive monitoring parameters followed prior to therapy through the development of pulmonary edema have been published.

Volume overload is implicated as the cause of pulmonary edema because β-adrenergic agents can cause fluid and sodium retention and potentiate volume overload via stimulation of the renin-aldosterone system.[28, 44] As a consequence of fluid retention, serum colloid oncotic pressure may be reduced changing the driving pressure across the pulmonary capillary membrane.[14] The role that concurrent steroid administration plays in the development of β-sympathomimetic-induced pulmonary edema is not clear because the steroids used most commonly in an effort to stimulate fetal lung maturity have very little mineralocorticoid activity. If cardiac decompensation does not occur and fluid volume is normal, a leaky pulmonary capillary membrane is left as an "explanation of exclusion" for pulmonary edema during tocolysis. A mechanism for β-stimulation causing capillary leak has not been proposed.

The metabolic effects of β-adrenergic tocolytic therapy include an increase in serum glucose concentration and a fall in potassium concentration.[14, 44, 61] This chain of events results from the stimulation of glycogenolysis and direct pancreatic stimulation. As serum glucose and insulin levels rise, potassium is driven intracellularly. It is generally recommended that serial electrolytes and glucose concentration be followed in patients on this therapy.[26] However, the administration of IV potassium in an attempt to achieve "normal" extracellular potassium levels is not recommended as total body stores are not depleted.

Magnesium Sulfate

Elevated serum levels of magnesium suppress the contractility of the myometrium. Magnesium sulfate ($MgSO_4$) infusion is employed as a tocolytic agent at some institutions. Preeclampsia is also treated with magnesium sulfate. The mechanism of tocolytic action is not thoroughly defined, though it appears that magnesium produces relaxation of the myometrium at the level of the muscle cell.[27] Magnesium is thought to be a competitive antagonist of calcium serving to decrease the levels of myoplasmic free calcium and thus inhibit myosin-actin interaction.[42]

Tocolytic effects are seen with magnesium levels in the 5 to 8 mg per dL range.[27, 42] Administration protocols employ a bolus dose followed by a continuous infusion to maintain therapeutic levels. A bolus of 4 to 6 g $MgSO_4$ IV given over 20 minutes followed by an infusion of 1 to 3 g per hour $MgSO_4$ IV usually produces therapeutic levels.[26, 42, 53] Magnesium levels should be checked every 6 to 8 hours during therapy, although clinical signs including the loss of patellar reflexes are a more sensitive indication of relative overdose in an individual.

Signs and symptoms of magnesium toxicity begin to manifest at serum levels above 9 mg per dL. Loss of deep tendon reflexes followed by respiratory, CNS, and cardiac depression occurs with progressive toxicity.[42] Excretion of magnesium is dependent on renal function. With normal kidney function, 75% of the magnesium is excreted during the infusion, and levels return to baseline within 24 hours after the discontinuation of the drug.[16] In the patient with renal impairment, close monitoring of serum levels as well as periodic physical examination are necessary to avoid toxicity.

Side effects are most common during the initial IV bolus administration of $MgSO_4$. Effects include flushing, headache, nystagmus, blurred vision, chest pain, nausea, dizziness, drowsiness, and dryness of the mouth.[21, 45] Magnesium is a CNS depressant and altered levels of consciousness may be observed. The cardiovascular consequences of carefully administered $MgSO_4$ are minimal. Studies in both animals and humans have noted only a mild transient fall in blood pressure, which generally returned to baseline in 1 hour.[13, 18] Bourgeois et al[6] reported two cases in which profound hypotension was seen with $MgSO_4$ therapy. In both cases it was thought that the preeclampsia-induced hypovolemia was the precipitating event.[6] Cardiac arrest has been reported in the setting of hypermagnesemia and presumed overdose.[37]

As with the β-sympathomimetic agents used for tocolysis, magnesium sulfate has been associated with cases of pulmonary edema. In a retrospective review, Elliott[21, 22] noted four cases of pulmonary edema in 355 patients (an incidence of approximately 1%). Other risk factors such as twin gestation, anemia, and pregnancy-induced hypertension may contribute to this occurrence.

The metabolic effects of magnesium administration include a fall in ionized and total calcium, an increase in parathyroid hormone, and little change in phosphate or calcitonin.[16, 17] The magnitude of this decrease in ionized calcium is 12 to 16% and it is primarily accounted for by urinary calcium excretion three times that of baseline.[16] The inhibitory effects of magnesium at the neuromuscular junction combined with a decrease in calcium may potentiate muscle relaxation.[24, 25, 41] Careful monitoring of the twitch response is recommended in patients who receive neuromuscular agents during magnesium therapy and documentation of a full reversal prior to extubation is mandatory.

Calcium gluconate should be readily available to treat toxicity. Otherwise, management of hypermagnesemia includes discontinuation of the infusion, documentation of the serum levels, and supportive therapy.

SUMMARY

Tocolytic and oxytocic therapies are widely used in contemporary obstetric practice. The anesthesiologist is often called upon to participate in the care of patients who are receiving uterotonic medications. In addition to their effects on the myometrium, each of these drugs has direct and indirect effects on a variety of organ systems. Oxytocin stimulates the uterus to contract via changes in intracellular calcium. Its direct vasodilating and antidiuretic properties lead to the possibility of hypotension or water overload. Ergotamines used for postpartum uterine atony carry the risk of generalized vasoconstriction and hypertension that may be life threatening. Prostaglandins of both the E and F classes stimulate uterine contractions. Side effects include nausea, vomiting, diarrhea, and hyperpyrexia. The two classes differ in their hemodynamic effects: prostaglandin E leads to a decrease in SVR and blood pressure with no change or a decrease in pulmonary vascular resistance; $PGF_{2\alpha}$ generates an increase in blood pressure, heart rate, cardiac output, and pulmonary vascular resistance. Prostaglandin $F_{2\alpha}$ also stimulates bronchoconstriction.

The most common tocolytics are β-sympathomimetics and magnesium sulfate. The side effects of β-adrenergic therapy arise from stimulation of both β_1 and β_2 receptors. Inotropic and chronotropic effects on the myocardium may be sufficient to cause ischemia. Pulmonary edema is associated with β-mimetic therapy. Glucose and electrolyte balance should be monitored during treatment. Magnesium sulfate decreases uterine tone probably by antagonizing calcium at the cellular level. As plasma levels increase, progressive depression of the respiratory, CNS, and cardiac systems follows. Toxic levels are more likely in the patient with renal function impairment. Calcium serves to reverse magnesium toxicity. Because of its effects at the neuromuscular junction, magnesium potentiates both depolarizing and nondepolarizing muscle relaxants.

Familiarity with the range of effects of these drugs should assist the anesthesiologist in providing safe passage for the pregnant patient and her fetus from the antepartum to postpartum period.

REFERENCES

1. Abdul-Karim R, Assali NS: Renal function in human pregnancy. J Lab Clin Med 57:522, 1961

2. Abouleish E: Postpartum hypertension and convulsion after oxytocic drugs. Anesth Analg 55:813, 1976
3. Amico JA, Seitchik J, Robinson AG: Studies of oxytocin in plasma of women during hypocontractile labor. J Clin Endocrinol Metab 58:274, 1984
4. Benedetti TJ, Hargrove JC, Rosene KA: Maternal pulmonary edema during premature labor inhibition. Obstet Gynecol 59:335, 1982
5. Bieniarz J, Ivankovich A, Scommegna A: Cardiac output during ritodrine treatment in premature labor. Am J Obstet Gynecol 118:910, 1974
6. Bourgeois FJ, Thiagarajah S, Harbert GM, et al: Profound hypotension complicating magnesium therapy. Am J Obstet Gynecol 154:919, 1986
7. Brooke OG, Robinson BF: Effect of ergotamine and ergometrine on forearm venous compliance in man. Br Med J 1:139, 1970
8. Browning DJ: Serious side effects of ergometrine and its use in routine obstetric practice. Med J Aust 1:957, 1974
9. Buxton A, Goldberg S, Hirshfeld JW, et al: Refractory ergonovine-induced coronary vasospasm: Importance of intracoronary nitroglycerin. Am J Cardiol 46:329, 1980
10. Casady GN, Moore DC, Bridenbaugh LD: Postpartum hypertension after use of vasoconstrictor and oxytocic drugs. JAMA 172:1011, 1960
11. Cates W, Grimes DA, Haber RJ: Abortion deaths associated with the use of prostaglandin $F_{2\alpha}$. Am J Obstet Gynecol 127:219, 1977
12. Cates W, Jordaan HVF: Sudden collapse and death of women obtaining abortions induced with prostaglandin $F_{2\alpha}$. Am J Obstet Gynecol 133:398, 1979
13. Cotton DB, Gonik B, Dorman KF: Cardiovascular alterations in severe pregnancy-induced hypertension: Acute effects of intravenous magnesium sulfate. Am J Obstet Gynecol 148:162, 1984
14. Cotton DB, Strassner HT, Lipson LG, et al: The effects of terbutaline on acid base, serum electrolytes, and glucose homeostasis during the management of preterm labor. Am J Obstet Gynecol 141:617, 1981
15. Creasy RK: Preterm labor and delivery. *In* Creasy RK, Resnik R (eds): Maternal-Fetal Medicine, ed 2. Philadelphia, Saunders, 1988, p 415
16. Cruikshank DP, Pitkin RM, Donnelly E: Urinary magnesium, calcium, and phosphate excretion during magnesium sulfate infusion. Obstet Gynecol 58:430, 1981
17. Cruikshank DP, Pitkin RM, Reynolds WA, et al: Effects of magnesium sulfate treatment on perinatal calcium metabolism. Am J Obstet Gynecol 134:243, 1979
18. Dandavino A, Woods JR, Murayama K, et al: Circulatory effects of magnesium sulfate in normotensive and renal hypertensive pregnant sheep. Am J Obstet Gynecol 127:769, 1977
19. Eggers TR, Fliegner JR: Water intoxication and syntocinon infusion. Aust NZ J Obstet Gynaecol 19:59, 1979
20. Eklund B, Carlson LA: Central and peripheral circulatory effects and metabolic effects of different prostaglandins given IV to man. Prostaglandins 20:333, 1980
21. Elliott JP: Magnesium sulfate as a tocolytic agent. Am J Obstet Gynecol 147:277, 1983
22. Elliott JP, O'Keeffe DF, Greenberg P, et al: Pulmonary edema associated with magnesium sulfate and betamethasone administration. Obstet Gynecol 134:717, 1979
23. Fester A: Provocative testing for coronary arterial spasm with ergonovine maleate. Am J Cardiol 46:338, 1980
24. Ghoneim MM, Long JP: The interaction between magnesium and other neuromuscular blocking agents. Anesthesiology 32:23, 1970
25. Giesecke AH, Morris RE, Dalton MD, et al: Of magnesium, muscle relaxants, toxemic parturients, and cats. Anesth Analg 47:689, 1968
27. Gonik B, Creasy RK: Preterm labor: Its diagnosis and management. Am J Obstet Gynecol 154:3, 1986
37. Harbert GM, Cornell GW, Thornton WN: Effect of toxemia therapy on uterine dynamics. Am J Obstet Gynecol 105:94, 1969
28. Hauth JC, Hankins GD, Kuehl TJ, et al: Ritodrine hydrochloride infusion in pregnant baboons. Am J Obstet Gynecol 146:916, 1983
29. Hendricks SK, Keroes J, Katz M: Electrocardiographic changes associated with ri-

todrine-induced maternal tachycardia and hypokalemia. Am J Obstet Gynecol 154:921, 1986

30. Heupler FA: Provocative testing for coronary arterial spasm: Risk, method and rationale. Am J Cardiol 46:335, 1980
31. Hosenpud JD, Morton MJ, O'Grady JP: Cardiac stimulation during ritodrine hydrochloride tocolytic therapy. Obstet Gynecol 62:52, 1983
32. Hughes WA, Hughes SC: Hemodynamic effects of prostaglandin E_2. Anesthesiology 70:713, 1989
33. Huszar G: Physiology of the Myometrium. *In* Creasy RK, Resnik R (eds): Maternal-Fetal Medicine, ed 2. Philadelphia, Saunders, 1988, p 141
34. Johnstone M: The cardiovascular effects of oxytocic drugs. Br J Anaesth 44:826, 1972
35. Katz M, Robertson PA, Creasy RK: Cardiovascular complications associated with terbutaline treatment for preterm labor. Am J Obstet Gynecol 139:615, 1981
36. Mantyla R, Kanto J: Clinical pharmacokinetics of methylergometrine. Int J Clin Pharmacol Ther Toxicol 19:386, 1981
37. McCubbin JH, Sibai BM, Abdella TN, et al: Cardiopulmonary arrest due to acute maternal hypermagnesaemia. Lancet 1:1058, 1981
38. Michalak D, Klein V, Marquette GP: Myocardial ischemia: A complication of ritodrine tocolysis. Am J Obstet Gynecol 146:861, 1983
39. Miller D, Waters DD, Warnica W, et al: Is variant angina the coronary manifestation of a generalized vasospastic disorder? N Engl J Med 304:763, 1981
40. Nakano J: Cardiovascular actions of oxytocin. Obstet Gynecol Surv 28:75, 1973
41. Partridge BL, Key T, Reisner LS: Life-threatening effects of intravascular absorption of prostaglandin $F_{2\alpha}$ during therapeutic termination of pregnancy. Anesth Analg 67:1111, 1988
42. Petrie RH: Tocolysis using magnesium sulfate. Semin Perinatol 5:266, 1981
43. Phelan JP, Meguiar RV, Matey D, et al: Dramatic pyrexic and cardiovascular response to intravaginal prostaglandin E_2. Am J Obstet Gynecol 132:28, 1978
44. Philipsen T, Eriksen PS, Lynggard F: Pulmonary edema following ritodrine-saline infusion in premature labor. Obstet Gynecol 58:304, 1981
45. Rall TW, Schleifer LS: Oxytocin, prostaglandins, ergot alkaloids, and other drugs; Tocolytic agents. *In* Gilman AG, Goodman LS, Rall TW, et al, (eds): The Pharmacological Basis of Therapeutics, ed 7. New York, Macmillan, 1985, p 926
46. Ringrose CAD: The obstetrical use of ergot: A violation of the doctrine "Primum non nocere". Can Med Assoc J 87:712, 1962
47. Saunders WG, Munsick RA: Antidiuretic potency of oxytocin in women postpartum. Am J Obstet Gynecol 95:5, 1966
48. Schwartz RH, Jones RWA: Transplacental hyponatremia due to oxytocin. Br Med J 1:152, 1978
49. Schwarz R, Retzke U: Cardiovascular effects of terbutalin in pregnant women. Acta Obstet Gynecol Scand 62:419, 1983
50. Secher NJ, Thayssen P, Arnsbo P, et al: Effect of prostaglandin E_2 and $F_{2\alpha}$ on the systemic and pulmonary circulation in pregnant anesthetized women. Acta Obstet Gynecol Scand 61:213, 1982
51. Smith AP: The effects of intravenous infusion of graded doses of prostaglandins $F_{2\alpha}$ and E_2 on lung resistance in patients undergoing termination of pregnancy. Clin Sci 44:17, 1973
52. Spielman FJ, Herbert WNP: Maternal cardiovascular effects of drugs that alter uterine activity. Obstet Gynecol Surv 43:516, 1988
53. Spisso KR, Harbert GM, Thiagarajah S: The use of magnesium sulfate as the primary tocolytic agent to prevent premature delivery. Am J Obstet Gynecol 142:840, 1982
54. Taylor GJ, Cohen B: Ergonovine-induced coronary artery spasm and myocardial infarction after normal delivery. Obstet Gynecol 66:821, 1985
55. Tye K, Desser KB, Benchimol A: Angina pectoris associated with use of terbutaline for premature labor. JAMA 244:692, 1980
56. US Department of Health and Human Services, Public Health Service, National Center for Health Statistics: Vital Statistics of the United States, 1980. Vol 1, Natality. Hyattsville, 1984

57. Wagner JM, Morton MJ, Johnson KA, et al: Terbutaline and maternal cardiac function. JAMA 246:2697, 1981
58. Weis FR, Markello R, Mo B, et al: Cardiovascular effects of oxytocin. Obstet Gynecol 46:211, 1975
59. Willis DC, Caton D, Levelle JP, et al: Cardiac output response to prostaglandin E_2-induced abortion in the second trimester. Am J Obstet Gynecol 156:170, 1987
60. Ying YK, Tejani NA: Angina pectoris as a complication of ritodrine hydrochloride therapy in premature labor. Obstet Gynecol 60:385, 1982
61. Young DC, Toofanian A, Leveno KJ: Potassium and glucose concentrations without treatment during ritodrine tocolysis. Am J Obstet Gynecol 146:105, 1983

Address reprint requests to

Stephanie A. Hughes, MD
Department of Anesthesiology, H-770
University of California, San Diego Medical Center
225 Dickinson Street
San Diego, CA 92103

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Systemic Analgesia in Labor

Still a Viable Option?

*Harold J. Heyman, MD**

Regional analgesia for pain relief in labor with continuous lumbar epidural blockade is a technique that is used with increasing frequency in large hospitals.[1] It is also being used more frequently in smaller community hospitals because of obstetrician and patient demands. Alternatives to lumbar epidural analgesia have been considered when regional anesthesia is contraindicated, or where manpower is not available to perform epidural analgesia. Also, many obstetricians and patients prefer a trial of alternative techniques for labor pain, before proceeding to regional analgesia. The alternative techniques to regional analgesia for labor pain include narcotics and tranquilizers, paracervical block, transcutaneous electrical nerve stimulation, and psychoprophylaxis (Lamaze).

Psychoprophylaxis has been effective in lessening labor pain. Lamaze training programs have promoted the concept that a parturient who is informed about maternal physiology and prepared for the laboring process by psychological conditioning and support will be less apprehensive and need little or no systemic medication. However, this technique depends on strong personal motivation of the parturient for success, and may be ineffective in situations involving long labors with strong contractions. Long, painful labors may cause the parturient to experience fatigue and anxiety. She may hyperventilate, developing respiratory alkalosis. This may lead to alveolar hypoventilation and hypoxemia between contractions. Maternal metabolic acidosis may result from decreased tissue perfusion secondary to hyperventilation-induced reduction in cardiac output. Catecholamine release may contribute to this by causing a decrease in tissue perfusion. Fixed acids then readily traverse the placenta, resulting in fetal metabolic acidosis.

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* Clinical Associate Professor, Department of Anesthesiology, University of Illinois College of Medicine; Director of Obstetric Anesthesia and Coordinator, Residency Education, Illinois Masonic Medical Center, Chicago, Illinois

Decreased uterine perfusion secondary to reduced maternal cardiac output contributes to fetal acidosis. Finally, maternal respiratory alkalosis may cause the maternal oxyhemoglobin dissociation curve to shift to the left, resulting in less oxygen transfer to the fetus. This causes a further increase in fetal metabolic acidosis. Timely administration of maternal analgesia, before excessive pain, anxiety, and fatigue supervene, may prevent the development of fetal acidosis from these causes. If fetal acidosis is already present, however, before maternal drug administration, placental transfer and "ion-trapping" of these drugs may be enhanced.

Transcutaneous electrical nerve stimulation is simple, noninvasive, and not associated with maternal or neonatal depression. Although it has provided some relief of low back pain during the first stage of labor, it has been ineffective with anterior abdominal pain or perineal pain during the second stage.

Paracervical block[12] is used in only about 5% of parturients because of reports of fetal bradycardia secondary to toxic fetal blood levels of local anesthetic or uterine artery spasm.

The use of narcotics and tranquilizers for labor analgesia is still the primary form of pain relief used in obstetrics in the United States.[12] The advantage of this technique lies in the simplicity and ease of administration, as well as minimal fluid preloading, patient monitoring, and complications. The disadvantages, specially compared with lumbar epidural analgesia, consist of inadequate pain relief, clouded sensorium, and the risk of maternal and neonatal respiratory depression. Systemic analgesics for labor became popular in the early 1900s when morphine was combined with scopolamine to produce "twilight sleep," a state that combined amnesia with analgesia. By the 1950s, narcotic, tranquilizer, and barbiturate mixtures were often administered in arbitrary combinations, excessive doses, and by uninformed personnel. In the past 30 years, significant advances have been made in the understanding of the modes of action, distribution, metabolism, excretion, and side effects associated with the use of tranquilizers and narcotics in the parturient and neonate. There has also been the development of new drugs and new modes of administration.

The ease of administration and few complications involving tranquilizer and narcotic drugs for labor analgesia is one reason that, in North American practice, they are usually ordered by labor and delivery personnel such as obstetricians, family practitioners, and nurse midwives, rather than by anesthesia personnel. The other reason is that in most hospitals, labor and delivery personnel have been more readily available for constant monitoring of patient progress than have anesthesia personnel. We will review the narcotics and tranquilizers that are currently used or have been used for analgesia in labor and delivery. One area that might provide a role for anesthesiologist involvement in a "nonepidural" analgesic technique for labor is ketamine analgesia for delivery.

NARCOTICS

Narcotics are the most commonly used and the most effective systemic medication for labor analgesia. Pain relief with these agents is dose-dependent, as are the undesirable side effects of respiratory depression, hypotension, nausea, and vomiting. The parturient obviously will not be able to walk about because of postural hypotension. Nausea and vomiting may be additive to that normally produced by the physiology of labor itself and may require treatment with phenothiazines or other related drugs. All narcotic agents cross the placenta[22] and may cause loss of beat-to-beat variability and neonatal respiratory depression. Normal beat-to-beat variability of the fetal heart rate reflects normal fetal brain function. Loss of this normal variability may occur during hypoxemia or acidosis. It may also occur following maternal drug administration. Changes in fetal heart rate variability following maternal drug administration must be recognized by labor and delivery personnel and included in their overall assessment of fetal well-being. Large doses may also cause sedation and obtundation of protective reflexes, as well as inhibition of uterine activity in the latent phase of labor. Cerebral depression may make the parturient unresponsive, uncooperative, and unable to fully participate in or enjoy the labor and delivery process. Such side effects, of necessity, dictate the judicious administration of limited doses, which often results in inadequate analgesia. Dosage limitation is included in the Guidelines for Perinatal Care,[14] published by the American Academy of Pediatrics and the American College of Obstetrics and Gynecology.

Although there are a large number of narcotics currently available in the United States, only a few of these are now used in obstetrics. These include meperidine (Demerol), fentanyl (Sublimaze), butorphanol (Stadol), and nalbuphine (Nubain). Certain narcotic agents, because of undesirable maternal or neonatal effects are no longer widely used. These include morphine and pentazocine (Talwin).

Morphine

Although some obstetricians still employ a small dose of morphine as a sedative during prodromal labor, the obstetric team now rarely uses this long-acting agent. In equianalgesic doses, it produces more neonatal respiratory depression than meperidine, possibly because morphine has a greater ability to penetrate the infant's brain.[34] The role of morphine analgesia in the parturient would be largely confined to its administration for post-cesarean section analgesia, as a patient-controlled analgesia (PCA) or as spinal morphine.

Alphaprodine

This narcotic agent formerly was popular for obstetric analgesia in labor, because of its rapid onset and shorter duration of action. Reports of maternal respiratory arrest after repeated doses have been reported with large doses, for example 30 to 40 mg IV. Smaller doses

(10 to 20 mg) have been used but at present, this drug is not commercially available.

Pentazocine

Pentazocine was the first of the agonist-antagonist group of agents to be introduced with the hope that it would combine potent analgesic effects with minimal respiratory depression and absence of addictive propensity. Unfortunately,[23] repeat doses may be associated with sigma-receptor stimulation, consisting of psychotomimetic effects, such as hallucinations and nightmares. Pentazocine is not likely to be used in obstetrics today, although its efficacy in labor has been established.

Meperidine

Meperidine has been the most frequently used narcotic-analgesic in the laboring patient. The peak effect occurs in 5 to 10 minutes after intravenous administration and 40 to 50 minutes after intramuscular administration. Its duration of action is 2 to 4 hours. The dose range commonly used is 50 to 100 mg IM or 12.5 to 25 mg IV. Neonatal depression following maternal meperidine administration may be manifested by low Apgar scores, prolonged time to sustained respiration, abnormal blood gases, and lowered neurobehavioral scores. One hundred milligrams of intramuscular meperidine[21] produced almost no neonatal depression, as manifested by decreased Apgar scores, if delivery occurred within 1 hour or 4 or more hours after administration. The incidence of neonatal depression was increased when delivery occurred within 2, 3, or up to 4 hours after administration. Shnider and Moya[33] found the greatest number of depressed neonates born 2 hours after intramuscular administration of 50 mg. These effects then are related to the dose and to the time interval between maternal administration and delivery of the neonate. These earlier studies appeared to show that both short or long drug-delivery intervals were less likely to result in neonatal drug depression following intramuscular administration. Intermediate drug-delivery intervals of up to 2, 3, or 4 hours following intramuscular administration resulted in the greatest decrease in Apgar scores. The delay in appearance of the neonatal depression with a short drug-delivery interval following intramuscular administration is most likely due to slow uptake. Neonatal depression was not seen[21] when 50 mg was administered intramuscularly to the mother 30 minutes before delivery.

In contrast to meperidine levels, Kuhnert et al[17] found that cord levels of normeperidine, a pharmacologically active metabolite of meperidine, reached their highest level many hours later. This metabolite has a half-life of 62 hours in the neonate. Kuhnert et al also found that the longest drug-delivery intervals following meperidine administration, in contrast to the situation with Apgar scores, resulted in the most abnormal neurobehavioral scores. These scores were measured at 12 hours and 3 days of age. It is thought normeperidine is responsible for these low neurobehavioral scores in neonates following the longest drug-delivery intervals. Normeperidine is a known central nervous system depressant. It is produced by hepatic N-demethylation of meperidine. This metabolite has significant analgesic and toxic properties and may be more powerful than meperidine itself. Interestingly, chronic administration of an enzyme-inducing agent, such as phenobarbital, will induce hepatic microsomal enzyme activity, which can enhance the neonatal toxicity of meperidine by increasing the production of normeperidine. It is believed, therefore,[18] that acute neonatal effects of maternal administration of meperidine, as manifested by decreased Apgar scores, are due to high tissue levels of meperidine, whereas the more subtle and prolonged effects on neurobehavior are due to normeperidine. Meperidine has also been administered during labor as part of a PCA technique.

Appraisal of Meperidine

Meperidine is easy to administer by labor and delivery personnel with few serious maternal side effects, making its administration by anesthesia personnel unnecessary. Although formerly the most popular drug used for analgesia during labor, the recent reports linking lowered neonatal neurobehavioral scores to prolonged intervals between maternal administration and delivery may cast a shadow over meperidine usage. This will cause obstetric personnel to seek other narcotic agents in its stead.

Fentanyl

Fentanyl is a rapidly acting narcotic analgesic. It is a synthetic opioid 1000 times as potent as meperidine. One hundred micrograms is equianalgesic to 10 mg of morphine. The usual doses are 12 to 50 μg IV. It is highly lipid soluble and has a rapid onset and short duration of action. Intravenously, it produces analgesia almost immediately, with a peak action in 3 to 5 minutes, and a 30- to 60-minute duration. The short duration of action is due to redistribution rather than rapid metabolism. Repeated doses, especially over 100 μg, tend to be accumulated in body fat stores, then re-released into the circulation. Fentanyl has been detected in fetal blood within 1 minute[7] after maternal administration, with peak levels in 5 minutes. When up to 1 μg per kg was administered intravenously to mothers during cesarean delivery, there were no adverse neonatal effects on Apgar scores, umbilical cord blood gases, or neurobehavioral scores. Because of its ability to cause sudden and profound respiratory depression along with strong analgesia, it has not been used by labor and delivery personnel for analgesia during labor.

Appraisal of Fentanyl

If fentanyl were to have a significant role in systemic analgesia during labor and delivery, it would have to be administered by anesthesia rather than labor and delivery personnel, to ensure adequate patient monitoring and safeguards. It could be administered late in labor for an out-of-control parturient or in the delivery room for brief, but painful procedures. Fentanyl is used more appropriately in continuous lumbar epidural analgesia, as an additive to the local anesthetic agents used in the epidural space.

Alfentanil

Alfentanil is a newly introduced ultrashort-acting synthetic opioid, with a fast onset and short duration. Early hopes were that, because alfentanil has a short duration of action in adults, this would also be true in the fetus and neonate. This has not yet been shown to be true. In fact, in sheep studies,[6] while maternal levels of alfentanil and sufentanil declined more rapidly than fentanyl following an intravenous bolus, fetal narcotic concentrations of alfentanil declined more slowly than fentanyl. Golub et al,[13] studying infant neurobehavioral development in monkeys after maternal exposure to alfentanil or meperidine, concluded that neurobehavioral development at 3 months of age was impaired to a greater extent after alfentanil than after meperidine. Chronic neurobehavioral impairment in these studies was not related to persistent blood levels of the drugs or their metabolites.

Appraisal of Alfentanil

At the present time, the use of alfentanil for obstetric analgesia during labor cannot be recommended.

Butorphanol and Nalbuphine

There has been considerable interest in finding a drug that would combine potent analgesic effects with minimal respiratory depression and other side effects. Pentazocine (Talwin) has not achieved this distinction. Two of the newer agonist-antagonist agents, butorphanol (Stadol) and nalbuphine (Nubain), provide good analgesia with minimal psychotomimetic effects due to sigma receptor stimulation. Butorphanol, 2 mg intramuscularly or 1 mg intravenously, produce respiratory depression equivalent to 10 mg of morphine. However, whereas larger doses of morphine produce more respiratory depression, increasing doses of butorphanol and nalbuphine do not,[11] the so-called "ceiling effect."[29] The proposed explanation for this effect is that they are strong kappa-receptor agonists and weak mu-receptor antagonists. There is also, however, a ceiling effect on analgesia. Maduska and Hajgassemali[20] found no difference in neonatal Apgar scores, time to sustained respirations, or cord blood gases in neonates exposed to either butorphanol, 1 to 2 mg, or meperidine, 40 to 80 mg. Quilligan et al[28] reported than 1 mg of butorphanol achieved more effective analgesia than meperidine, 40 mg at 30 to 60 minutes after administration. Butorphanol may also be associated with fewer side effects such as nausea, vomiting, and dizziness than meperidine. Wilson et al[35] evaluated the use of nalbuphine given intravenously during active labor. He found no neonatal depression in this group of patients given 15 to 20 mg nalbuphine during active labor. The main side effect associated with both butorphanol and nalbuphine is drowsiness. Occasionally, mild psychotomimetic effects can occur, but certainly not ones as severe as those seen with pentazocine. Butorphanol,[26] but not nalbuphine, may increase pulmonary vascular resistance and myocardial work.

Appraisal of Butorphanol and Nalbuphine

The presence of a ceiling effect on maternal respiratory depression and absence of metabolites with neonatal depressant effects of their own, make these drugs among the more desirable narcotic-type drugs introduced so far in obstetrics for systemic analgesia. They are easy to administer and monitor by labor and delivery personnel themselves; there would seem to be little role for anesthesia personnel in their administration. Maternal drowsiness does occur, however, and inadequate analgesia due to the ceiling effect could be a major disadvantage.

PATIENT-CONTROLLED ANALGESIA

The commonest means of narcotic administration during labor is by the intravenous or intramuscular route. This results in a bolus dose of narcotic to the mother with accompanying side effects when the blood level of the narcotic is high. PCA or small doses of intravenous narcotic administered on demand has achieved considerable success in postoperative analgesia, including post-cesarean–section analgesia. PCA contains a syringe delivery and control system. The parturient can trigger her own release of a small dose of narcotic in response to pain by pushing a hand-held button. A "lockout period" is preset in order to render the apparatus inoperable for a certain interval, preventing self-administration of excessive doses. Nalbuphine administration has been compared by PCA versus intermittent bolus doses.[25] Patients receiving nalbuphine by PCA had less drowsiness and were more satisfied with their analgesia than those in the intermittent dose group. The mean total dose of nalbuphine and the request for antiemetic medications was lower in the PCA group, and there was no difference in neonatal Apgar scores. A study[9] comparing intramuscular meperidine to PCA meperidine found improved patient satisfaction in the PCA group, with similar umbilical vein drug concentrations, Apgar scores, and cord blood gases in the two groups.

Appraisal of PCA

These clinical studies evaluating the use of PCA suggest that this method of providing analgesia may enable the mother to tailor her analgesic needs as labor progresses. PCA, especially when provided with butorphanol or nalbuphine, may provide a stable level of analgesia, avoid high blood levels of narcotic, and have few side effects. PCA is easy to set up and administer by labor and delivery personnel, and requires little in the way of monitoring. The services of anesthesia personnel are unlikely to be needed when this technique is used. PCA may provide better pain relief with less medication. There may be greater parturient satisfaction with this self-controlling type of device as opposed to intramuscular or intravenous administration. High hospital and patient cost may be a deterrent to its use. Before PCA comes into standard use in the labor and delivery area, further investigation into its effects on maternal safety and neonatal outcome will be necessary.

BARBITURATES

Secobarbital (Seconal) and pentobarbital (Nembutal) may be used during the latent phase of labor to provide sedation and relaxation. Occasionally, they are used to "rest" the patient overnight following a "failed induction," in preparation for a repeated attempt the next day. If given 12 to 24 hours prior to delivery in this way, they do not seem to be associated with neonatal depression. Barbiturates rapidly cross the placenta and can be associated with neonatal depression if given[30] during the active phase of labor. Barbiturates may also produce a paradoxical antianalgesic effect in the presence of pain. This may be manifested by excitement, restlessness, and disorientation.

Appraisal of Barbiturates

The role of barbiturates in the parturient is strictly limited to an early latent labor, or when she requires overnight rest prior to restarting induction in the morning.

TRANQUILIZERS

Tranquilizers may be beneficial to the mother during labor because they relieve anxiety; some of these drugs also have antiemetic properties.

Benzodiazepines

These drugs have anxiety-relieving, sedative, hypnotic, amnestic, anti-convulsant, and muscle relaxant properties.

Diazepam (Valium)

This drug has been well studied in obstetrics. It rapidly crosses the placenta[3] and fetal blood levels may exceed maternal levels. Small doses of 2 to 5 mg IV in labor,[31] however, may have minimal effects except for decrease in the beat-to-beat variability of the fetal heart rate and lowering of neonatal temperature. Large doses of diazepam have been given intravenously during labor to control seizures in an eclamptic patient. If the total dose administered to the mother exceeds 30 mg, the drug and its metabolites may persist in the newborn for days[5, 10] producing hypotonia, hypoactivity, poor sucking reflex, and hypothermia. Large doses of intravenous diazepam may also interfere with bilirubin binding to albumin in the newborn and therefore increase the susceptibility of the infant to kernicterus.[32] This is unlikely with a dose of 5 mg or less. Diazepam also causes burning along the course of the vein when injected; thrombophlebitis also has been reported along the venous injection site.

Appraisal of Diazepam

Even though small intravenous doses of diazepam have been used without significant adverse neonatal effects, it is likely that this agent will infrequently be used prior to delivery. Reports of deleterious neonatal effects of larger doses, burning pain on injection, and incidence of thrombophlebitis at the venous injection site, make other agents more desirable.

Midazolam

Midazolam is a water-soluble benzodiazepine with approximately twice the potency of diazepam, no active metabolites, and a shorter duration of action. The lack of thrombophlebitis at the venous site is also a desirable feature. It can also be administered intramuscularly as well as intravenously. After intravenous injection, effects are seen almost immediately and peak in about 3 minutes. Although it rapidly crosses the placenta,[4] adverse neonatal effects have to this date not been reported, perhaps because of its short duration of action and lack of toxic metabolites.

Appraisal of Midazolam

Although midazolam produces excellent relief of anxiety and would appear to have few fetal-neonatal effects because of its short duration of action, it has little to recommend it for sedation for labor and delivery. For most parturients, drug-induced amnesia for the events of labor and delivery would, today, not be considered a desirable experience. Although it is supposed to have anticonvulsant properties, it apparently has precipitated seizures in parturients with no seizure history.[8] It may play a small role as part of an intravenous sedation technique in cases requiring manual removal of the placenta. Its primary use is relegated to maternal sedation during cesarean delivery. Even in this situation[2, 15] in order to avoid maternal amnesia for delivery of the neonate, its administration should be delayed until the pediatricians have completed their ministrations to the baby, and it is brought over and shown to the mother at the head of the operating table.

Promethazine and Hydroxyine

Promethazine (Phenergan) and other phenothiazine derivatives are often used by labor and delivery personnel to provide sedation, allay anxiety, and reduce nausea and vomiting. Hydroxyzine (Vistaril), although not chemically related to the phenothiazines, has similar anxiolytic and sedative properties. These agents are commonly administered along with narcotics and can improve maternal sedation and relieve anxiety without causing neonatal depression.[27, 36] They can alter beat-to-beat variability of the fetal heart rate. In one study[27] comparing intramuscular meperidine 50 mg with meperidine 50 mg plus promethazine 50 mg, even though maternal sedation was increased in the group, which included promethazine, the incidence of depressed newborns was not increased. Also, the addition[1] of hydroxyzine 50 mg to a narcotic increased sedation without increasing neonatal depression.

Appraisal of Promethazine and Hydroxyzine

In the past, these agents were commonly ordered by labor and delivery personnel and administered in an intramuscular dose along with meperidine by labor and delivery nurses. Anesthesia personnel were not required for administration of these agents. With the introduction of the agonist-antagonist agents, butorphanol and nalbuphine, to obstetric practice, with their additional sedative properties, the need for meperidine combinations with promethazine or hydroxyzine has largely been obviated.

Ketamine

Ketamine (Ketalar, Ketaject) is a so-called "dissociative anesthetic" that produces intense analgesia, along with light sleep and preservation of spontaneous ventilation. Ketamine crosses the placenta rapidly[16, 19] but does not produce neonatal depression unless doses of 1 mg per kg are exceeded. At higher doses, low Apgar scores and neonatal hypertonia have resulted. Ketamine in low doses (10 to 15 mg) intravenously can be given to produce maternal anagesia without loss of consciousness.[24] This dose can be repeated every 3 to 5 minutes, but should not exceed 100 mg over a 30-minute period, in order to avoid maternal hallucinations or loss of consciousness. Higher doses also predispose to a regurgitation-aspiration risk. In the low-dose mode of administration, ketamine may be useful during difficult vaginal deliveries in anxious parturients, as a supplement to pudendal block, or a marginally functional epidural block.

Appraisal of Ketamine

Ketamine analgesia for vaginal delivery is one mode of systemic analgesia for labor and delivery that provides a necessary role for anesthesia personnel in its administration.

SUMMARY AND CONCLUSION

Systemic analgesics are still a viable option in labor and delivery. Despite recent ACOG-ASA recommendations that they consolidate, there still are a multitude of small labor and delivery units across the United States wherein access to services of anesthesia personnel capable of providing epidural analgesia for routine labor and delivery cases will be difficult to provide. In these situations systemic analgesia, although not providing as optimal a degree of analgesia as that by epidural block, can be reasonably and safely provided by labor and delivery personnel. They can use the newer drugs, butorphanol and nalbuphine, which provide analgesia with minimal fetal depression. The obvious drawback to this systemic analgesia technique is maternal somnolence, which makes it inferior to the continuous lumbar epidural analgesia technique. Maternal sedation with butorphanol or nalbuphine can also be instituted in an earlier stage of labor, before epidrual block is provided. PCA is a new and growing mode of analgesia administration. It is likely that it will continue to gain in popularity for labor analgesia, especially with the use of drugs such as butorphanol or nalbuphine. It is not likely, however, that anesthesia personnel will be required for PCA administration. Anesthesia personnel involvement in systemic analgesia for labor and delivery will more likely be confined to administration of low-dose ketamine for difficult vaginal delivery in anxious parturients, where regional anesthesia has not been used or is of insufficient quality.

REFERENCES

1. Brelje MC, Garcia-Brunuel R: Meperidine-hydroxyzine in obstetric analgesia. Obstet Gynecol 27:350–354, 1966
2. Camann W, Cohen MB, Ostheimer GW: Is midazolam desirable for sedation in parturients? Anesthesiology 65:441, 1986
3. Cavanagh D, Condo CS: Diazepam: A pilot study of drug concentrations in maternal blood, amniotic fluid and cord blood. Curr Ther Res 6:122–126, 1964
4. Conklin KA, Graham CW, Murad S, et al: Midazolam and diazepam: Maternal and fetal effects in the pregnant ewe. Obstet Gynecol 56:471–474, 1980
5. Cree IE, Meyer J, Hailey DM: Diazepam in labour: Its metabolism and effect on the clinical condition and thermogenesis of the newborn. Br Med J 4:251–255, 1973
6. Eisele JH: The use of short acting narcotics in obstetric anesthesia and the effects on the newborn. *In* Opioids in Anesthesia. Boston, Butterworth, 1984, p 102
7. Eisele JH, Wright R, Rogge P: Newborn and maternal fentanyl levels at cesarean section. Anesth Analg 61:179–180, 1982
8. Engstrom RH, Cohen SB: A complication associated with the use of midazolam. Anesthesiology 70:719, 1989
9. Evans JM, Rosen M, McCarthy J, et al: Patient-controlled intravenous narcotic administration during labour. Lancet 906–907, 1976
10. Flowers CE, Rudolph AJ, Desmond MN: Diazepam (Valium) as an adjunct in obstetric analgesia. Obstet Gynecol 34:68–81, 1969
11. Gal TJ: Analgesic and respiratory depressant activity of nalbuphine: A comparison with morphine. Anesthesiology 55:367–374, 1982
12. Gibbs CP, Krischer J, Peckham BM, et al: Obstetric anesthesia: A national survey. Anesthesiology 65:298–306, 1986
13. Golub MS, Eisele JH, Donald JM: Obstetric analgesia and infant outcome in monkeys: Infant development after intrapartum exposure to meperidine or alfentanil. Am J Obstet Gynecol 159:1280–1286, 1988
14. Guidelines for Perinatal Care, ed 2. American Academy of Pediatrics. American College of Obstetricians and Gynecologists, 1988, pp 63–64
15. Heyman HJ, Salem MR: Is midazolam desirable for sedation in parturients (letter-reply). Anesthesiology 66:577, 1987
16. Janeczko GF, El-Etr AA, Younes S: Low-dose ketamine anesthesia for obstetrical delivery. Anesth Analg 53:828–831, 1974

17. Kuhnert BR, Kuhnert PM, Tu AL, et al: Meperidine and normeperidine levels following meperidine administration during labor II. Fetus and neonate. Am J Obstet Gynecol 133:909–914, 1979
18. Kuhnert BR, Linn BL, Kennard MJ, et al: Effects of low doses of meperidine on neonatal behavior. Anesth Analg 64:335–342, 1975
19. Little B, Chang T, Chucot L, et al: Study of ketamine as an obstetric agent. Am J Obstet Gynecol 113:247–260, 1972
20. Maduska AL, Hajgassemali MA: A double blind comparison of butorphanol and meperidine in labour: Maternal pain relief and effect on the newborn. Can Anaesth Soc J 25:398–404, 1978
21. Mather LE, Lindop MJ, Tucket GT, et al: Pethidine revisited: Plasma concentration and effects after intramuscular injection. Br J Anaesth 47:1273, 1975
22. Moya F, Thorndike V: Passage of drugs across the placenta. Am J Gynecol 84: 1778–1798, 1962
23. Paddock R, Beer EG, Bellville JW, et al: Analgesic and side-effects of pentazocine and morphine in a large population of postoperative patients. Clin Pharmacol Ther 10:355–365, 1969
24. Pelz B, Sinclair DM: Induction agents for cesarean section: A comparison of thiopentone and ketamine. Anaesthesia 28:37–42, 1973
25. Podlas J, Bredland BD: Patient-controlled analgesia with nalbuphine during labor. Obstet Gynecol 70:202–204, 1987
26. Popio KA, Jackson DH, Ross AM, et al: Hemodynamic and respiratory effects of morphine and butorphanol. Clin Pharmacol Ther 23:281–287, 1978
27. Powe CE, Kiem IM, Fromhagen C, et al: Propiomazine hydrochloride in obstetric analgesia. JAMA 181:290–294, 1962
28. Quilligan E, Keegan KA, Donahue MJ: Double blind comparison of intravenously injected butorphanol and meperidine in parturients. Int J Gynaecol Obstet 18:363–367, 1980
29. Romagnoli A, Keats AS: Ceiling effect for respiratory depression by nalbuphine. Clin Pharmacol Ther 27:478–485, 1980
30. Root B, Eichner E, Sunshine I: Blood secobarbital levels and their clinical correlation in mothers and newborn infants. Am J Obstet Gynecol 81:948–956, 1961
31. Scher J, Hailey DM, Beard RW: The effects of diazepam on the fetus. J Obstet Gynaecol Br Comm 79:635–638, 1972
32. Schiff D, Chan G, Stern L: Fixed drug combinations and the displacement of bilirubin from albumin. Pediatrics 48:139–141, 1971
33. Shnider SM, Moya F: Effects of meperidine on the newborn infant. Am J Obstet Gynecol 89:1009–1015, 1964
34. Way WL, Costley EC, Way EL: Respiratory sensitivity of the newborn infant to meperidine and morphine. Clin Pharmacol Ther 6454–6461, 1965
35. Wilson SJ, Errick JK, Balkon J: Pharmacokinetics of nalbuphine during parturition. Am J Obstet Gynecol 155:340–344, 1986
36. Zsigmond E, Patterson RL: Double blind evaluation of hydroxyzine hydrochloride in obstetric anesthesia. Anesth Analg 46:275–280, 1967

Address reprint requests to

Harold J. Heyman, MD
Department of Anesthesia
Illinois Masonic Medical Center
836 West Wellington
Chicago, IL 60657

Obstetric Anesthesia 0889–8537/90 $0.00 + .20

Epidural Analgesia for Labor and Delivery

*Mary Jo A. Curran, MD**

Epidural anesthesia is the paramount technique for the relief of pain during labor and delivery. It is safe for both mother and baby and may actually improve the fetal intrauterine environment. It can transform a very painful and anxiety-provoking experience into one that is pleasant and positive. Its advantages over other types of pain relief are well recognized. However, it does require a significant amount of time and personnel. In the United States, 16% of all laboring patients receive epidural analgesia[25] but the rates are much greater in large centers. An obstetric anesthesia service that does not offer epidural analgesia for labor is incomplete. By providing epidural analgesia to the laboring patient, the anesthesiologist makes the most important contribution that he or she can make to alleviate the pain of childbirth. It is the one area of anesthesiology that provides immediate gratification to both the anesthesiologist and the patient.

HISTORY

The caudal approach to epidural anesthesia was introduced by Sicard and Cathelin in 1901. In 1921, Pages described the lumbar approach to epidural anesthesia but it was Dogliotti who made it popular. Hingson and Edwards introduced continuous caudal analgesia in the United States in 1942. In 1949, Cleland described the use of a two-catheter technique to alleviate labor pain. One catheter was placed in the upper lumbar or thoracolumbar region, which blocked the pain pathways associated with the first stage of labor, and a second catheter was placed through the sacral hiatus into the caudal canal to relieve the pain of the second stage. He had previously described, in

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* Attending Physician, Director of Obstetric Anesthesia, Michael Reese Hospital and Medical Center; Assistant Professor of Anesthesiology, University of Illinois, College of Medicine, Chicago, Illinois

1933, the pain pathways involved in labor. The first stage was blocked by paravertebral injections of local anesthetics of the 11th and 12th thoracic nerves and relief of the second stage pain was achieved by blockade of the sacral nerves. Cleland also noted that satisfactory sacral analgesia would be obtained by the injection of small doses of local anesthetics through lumbar epidural catheters in the sitting position in those patients in whom it was technically difficult to place a caudal catheter.[12]

The use of epidural anesthesia for obstetrics became popular in the 1950s. Many anesthesiologists found the double catheter technique cumbersome and preferred the use of the single lumbar catheter. Reports of inadequate analgesia for the second stage soon appeared and the lumbar approach to the epidural space for vaginal delivery was abandoned in favor of the caudal technique. Large volumes of local anesthetics, up to 30 mL of 2% lidocaine for caudal analgesia, were recommended and used. However, in the 1950s and 1960s attention to neonatal behavior and acid-base status disclosed that high concentrations of local anesthetics in the baby were associated with neonatal depression. It was also observed during this time that the parturient required lower doses of local anesthetics to achieve segmental blockade than her nonpregnant counterpart.[12] Contrary to the previous reports that a lumbar epidural catheter would not provide adequate perineal anesthesia, it was noted that small doses of local anesthetics through the lumbar catheter would ensure good pain relief of the second stage. The lumbar approach became the preferred technique over caudal and is almost exclusively used today. It is technically easier to perform in the pregnant patient, requires a smaller volume of local anesthetic, has a technical failure rate significantly lower than that of caudal, and a more predictable cephalad spread.[44]

ANATOMY OF PAIN PATHWAYS

The description of the sensory pathways by Cleland in 1933 is accepted today. The afferent sensory fibers from the entire uterus, including the cervix, are the A delta and C fibers that travel with the sympathetic nerves.[11] The fibers pass into the lumbar and lower thoracic sympathetic ganglia. The central connection is via the white rami communicans of the thoracic nerves 11 and 12, the posterior roots of these nerves, and the spinal cord. Blockade of T11 and T12 relieves the abdominal component of pain but as labor progresses patients may complain of severe backache. This seems to be due to recruitment of fibers from T10 and L1. Pain is felt in the lower abdomen, lower lumbar, sacral, and groin areas. The cutaneous distribution of these nerves is 8 to 10 cm caudal to their origin, which may explain why the parturient complains of pain in these areas. The most painful part of labor seems to be at the end of the first stage. It is unknown why uterine contractions are painful. Dilatation of the cervix and lower uterine segment is the accepted explanation.

Table 1. *Pain Pathways of Labor and Delivery*

First stage	
Early labor	T11–12
Later labor	T10–L1
Second stage	T10–L1 S2–4

In the second stage of labor, impulses are conducted via sacral nerves 2, 3, and 4 (the pudendal nerves), as well as via the pain pathways associated with the first stage. Pain of the second stage is often less severe than the first stage. The cervix is fully dilated and the intensity of the pain lessens. At this time the patient is involved in pushing and may be less focused on the pain. Some patients experience rectal pain during the latter part of labor, which is not blocked by epidural analgesia. This phenomenon is not well understood (Table 1).

The parasympathetic nerves of the pelvis are involved in Ferguson's reflex. Stimulation of this plexus increases uterine activity in animals and may also in humans.

PHYSIOLOGICAL CONSIDERATIONS OF EPIDURAL ANALGESIA

Catecholamine Levels and Uterine Blood Flow

The pain, anxiety, and physical exertion of labor produces widespread catecholamine release (Table 2). Stress induced in pregnant

Table 2. *Epidural Anesthesia for Labor and Delivery*

- Advantages
  - Provides excellent anesthesia
  - Increases maternal oxygen saturations
  - Increases uteroplacental blood flow, normal and preeclamptics
  - Improves neonatal acid-base status
  - Improves dysfunctional labor
  - Allows a more controlled delivery
  - Convert to use for cesarean section
  - No neonatal depression
  - An awake mother
- Disadvantages
  - Prolongs second stage
  - Higher incidence of instrumental delivery
  - Risks inherent to epidural anesthesia
    - Hypotension
    - Dural puncture headache
    - Intravascular/subarachnoid injection
    - Other rare neurologic complications

ewes was associated with an increase in norepinephrine levels, increased maternal mean arterial pressure, and a concomitant decrease in uterine blood flow.[55] Increased levels of maternal catecholamines are associated with decreased uterine blood flow and deleterious fetal effects. Studies using the radioactive xenon-133 clearance techniques to measure intervillous blood in the parturient during the first stage of labor demonstrate an increase in uterine blood flow after epidural analgesia. A properly administered epidural anesthetic using 10 ml of 0.25% bupivacaine or 2% 2-chloroprocaine is associated with a 35% increase in intervillous blood flow in healthy laboring parturients.[30] However, this same group showed no change in uterine blood flow during normal labor using 4 ml of 0.5% bupivacaine (20 mg) and 0.5% bupivacaine with epinephrine 20 μg.[33] It is presumably the greater sympathetic blockade associated with the greater mass of bupivacaine that caused a significant increase in placental blood flow. There was an even greater increase in intervillous blood in patients with severe preeclampsia. Ten ml of 0.25% bupivacaine produced a 77% increase in intervillous blood flow.[35] When a stable mean arterial blood pressure is maintained, placental blood flow is increased by either a reduction in extrinsic vascular tone (uterine tone) or a decrease in intrinsic vascular resistance (placental vasodilatation). Because there is no change in the resting tone of the uterus, there is presumed to be a decrease in the intrinsic vascular resistance of the placental bed.

Catecholamine levels during labor are reduced by the induction of epidural analgesia.[56] Epinephrine and norepinephrine plasma levels are significantly higher during labor than during the last trimester of pregnancy.[38] Those patients who are more anxious have higher levels of catecholamines and decreased uterine activity, as well as longer labors.[39] The mechanism by which the catecholamine level is reduced is related to the relief of maternal pain and not to the denervation of the adrenal medulla. Spinal anesthesia to the fourth thoracic dermatomal level significantly decreased the catecholamine levels in pregnant patients who were in labor. There was no change in catecholamine levels in patients who were not in labor.[2] This suggests that the alleviation of psychological and physical stress associated with painful uterine contractions is responsible for the decrease in plasma catecholamines.

It is concluded that the sympathectomy and relief of pain and anxiety with the resultant decrease in plasma catecholamines restores uterine blood flow to its nonstressed level.

Effect on Maternal Oxygen Saturation and Neonatal Acid-Base

Respiratory changes during pregnancy include an increase in tidal volume and ventilatory rate. This increase in minute ventilation causes lower P_{CO_2} levels (32 ± 2 torr) in term parturients compared with nonpregnant controls. This increase in alveolar ventilation results in an increased arterial oxygenation (106 ± 8 torr). Pain usually causes the pregnant patient to hyperventilate, which shifts the oxyhemoglobin dissociation curve to the left. This increases the maternal oxygen affinity and makes the unloading of oxygen to the fetus less favorable.

Hypoventilation follows these episodes of hyperventilation and decreases maternal arterial oxygen tension. A study that measured maternal oxygen saturation by pulse oximetry showed a statistically significant decrease in oxygen saturations and neonatal acid-base status in primiparas treated with meperidine and nitrous oxide when compared with a group receiving epidural analgesia. Among primiparas treated with epidural analgesia, there was an insignificant decrease in arterial oxygen saturation to 94 ± 1.3% (compared with a pregnant control group of patients not in labor). There were highly significant differences between the oxygen saturations of the epidural group compared with the meperidine and nitrous oxide group whose per cent oxygen saturation was 88.8 ± 3.9% (range 74 to 100%). The mean umbilical artery pH in neonates of primiparas with epidural anesthesia was 7.29 ± 0.06, compared with 7.21 ± 0.10 in those primiparas receiving meperidine and nitrous oxide, a statistically significant difference. The Apgar scores were not significantly different between the groups. Also, the group that received meperidine and nitrous oxide had significantly higher pain scores.[23] It was concluded that the significant decrease observed in maternal oxygenation and its effects on neonatal acid-base status are probably pain-mediated, as indicated by a close correlation between the pain scores during labor and delivery and the differences between the groups after delivery. However, in the multiparous groups, there was no difference in pain scores, maternal oxygen saturations, and neonatal acid-base values, which further supports these findings.

Cardiovascular Effects

The hemodynamic effects associated with epidural analgesia for labor and delivery may represent a great hazard for mother and baby. Most of the effects are caused by blockade of the sympathetic fibers. Sympathetic blockade results in vasodilatation of the resistance and capacitance blood vessels. There is venous pooling and a decrease in venous return to the heart. The cardiovascular complications of epidural blockade are often preventable. Aortocaval compression in the term parturient is the rule and not the exception. It is the most dangerous vascular feature of the pregnant patient. When venous return is reduced the arterial blood pressure may remain normal because of an increase in vascular resistance. Large reductions in cardiac output can occur without a decrease in blood pressure (mean arterial blood pressure = cardiac output × systemic vascular resistance). Blood pressure measurements are most commonly taken in the arm. The pressure of the upper extremities may be normal while that of the lower body is decreased due to a decreased cardiac output and a decreased vascular resistance. Occasionally there is an abnormal fetal heart tracing after epidural blockade in the presence of a normal maternal blood pressure. This is presumably due to a decreased cardiac output causing a decrease in uteroplacental blood flow or possibly uterine artery vasoconstriction. This effect is usually transient and not significant.[3, 4] The following measures are performed to maintain or improve cardiac output.

Prevention and Treatment. All patients receiving epidural analgesia should receive an intravenous volume load of a glucose-free balanced salt solution. Five-hundred to 1000 ml of lactated Ringer's solution or 0.9% NaCl are commonly used. A rapidly infused glucose load may cause maternal and neonatal hyperglycemia with subsequent neonatal hypoglycemia. Care must be taken in volume loading the patients who are receiving beta agonists and those with severe preeclampsia because they are more prone to develop pulmonary edema. This fluid bolus needs to be given acutely within 20 to 30 minutes of the sympathetic blockade. To avoid aortocaval compression, left uterine displacement is provided by placing a wedge under the right hip or having the patient assume the left or right lateral decubitus position. A systolic blood pressure of less than 100 mm Hg or a decrease of more than 25% needs to be treated. If mild maternal hypotension occurs, the treatment is more left uterine displacement or a lateral decubitus position (if not already in this position) and a rapid infusion of 200 to 300 mL of intravenous fluids. A slight head-down position will improve cardiacvenous return. Ephedrine 5 to 10 mg may be necessary if the hypotension does not respond rapidly to these measures or there is fetal compromise as seen by bradycardia or late decelerations. Ephedrine crosses the placenta and increases fetal heart rate and variability. These changes do not seem to be harmful to the fetus, but they may make the interpretation of the fetal tracing confusing. Oxygen needs to be given in cases of fetal distress after epidural induction.

Decreased Epidural Dose Requirement in the Parturient

In the 1960s, Bromage[12] found that the term parturient requires about a third less local anesthetic in the epidural space than the nonpregnant control. It was thought that the epidural space was smaller in pregnancy at term because of the engorged epidural veins. A given amount of local anesthetic would have a greater spread. Pregnant patients have a decrease in the dose requirements to about the same degree for general anesthesia. It has since been demonstrated that neural tissue in the pregnant patient is more sensitive to the effects of local anesthetics. It is believed that metabolic or hormonal changes are also responsible.

Effects of Epidural Analgesia on the Progress of Labor

Epidural anesthesia is often requested by the obstetricians for their patients with dysfunctional labor who require augmentation of labor with oxytocin. Oxytocin causes uterine contractions to be more intense and painful. An epidural anesthetic relieves this pain. However, the anesthesia may then be attributed to being the cause of a prolonged labor.

There are direct effects of local anesthetics on uterine tone, activity, and blood flow. Greiss et al[27] demonstrated a dose-dependent increase in uterine tone and a decrease in uterine blood flow when mepivacaine was systemically injected in pregnant sheep. Local anesthetics cause vasoconstriction when applied in vitro to human artery segments.[18] In clinical doses, there does not seem to be a significant effect on uterine blood flow. It would require a large intravascular injection of a local anesthetic to achieve blood levels capable of decreasing uterine blood flow and increasing uterine tone.

Numerous studies have been published about the effect of epidural analgesia on the progress of labor. There are many variables that affect the course of labor. These include size and position of the fetus, supine hypotension, maternal pain, level of catecholamines, polyhydramnios, parity of the mother, spinal reflexes, use of oxytocin, and the concentrations and volumes of the local anesthetics used in epidural anesthesia, to name a few. It is difficult to control for many of the variables involved in labor, and therefore makes the interpretation of many of these studies confusing and seemingly contradictory.

Phillips constructed labor curves of 598 patients receiving lumbar epidural anesthesia for labor. Patients received bupivacaine 0.125% with epinephrine 1:200,000. There was no difference in the first stage of labor for nulliparous and multiparous patients.[49] Jouppilla et al[34] showed no change in the first stage of labor in a prospective study of 100 patients receiving low-dose segmental analgesia (0.5% bupivacaine, 4 ml initial dose and repeated as needed) compared with a group receiving meperidine.[34] Others have also showed that once labor is established, epidural anesthesia can actually accelerate labor in patients who had previously demonstrated a dysfunctional labor pattern.[10] There are several other studies that have shown that there is no slowing of the progress of labor of the first stage when patients are in the lateral position and hypotension is avoided.

There are reports of a transient decrease in the progress of the first stage of labor. The causes of this finding may be the effects of epinephrine used in the local anesthetic solution producing a decrease in uterine activity, primarily a decrease in intensity without a change in frequency.

More controversial is the effect of epidural block on the second stage of labor. Some obstetricians request that the epidural analgesia be allowed to wear off during the second stage. It has never been shown that patients push more effectively when in pain. In fact, the opposite has been demonstrated. In 1983, Phillips and Thomas[50] showed that in primigravidas, there was a nonsignificant increased incidence of forceps use (43 versus 25%) and statistically significant incidence of persistent malrotations (4 versus 0) in a group that received no additional local anesthetic when the cervix was fully dilated compared with a group that received top-up doses for 0.25% bupivacaine (6 mL). There was no difference in the durations of the first and second stages.[50]

Naulty et al,[46] in 1988, instituted an abrupt change in epidural technique at their institution. After establishing epidural blockade with 10 mL of 0.25% bupivacaine and 50 μg of fentanyl, analgesia was maintained until delivery with 0.125 to 0.25% bupivacaine and fentanyl 2 μg per mL. They retrospectively evaluated patients who had received 1.5% lidocaine with epinephrine and received intermittent boluses of 1.5% lidocaine or 0.25 to 0.5% bupivacaine. No additional doses were given after full cervical dilatation. They found there was a statistically significant decrease in the cesarean section rate in the current group in whom analgesia was maintained until delivery. The incidence of forceps use also decreased from 17% in the group in which the epidural analgesia was allowed to wear off, to 6% in the more recent group.[46] The limitation of this study is that it is retrospective and there may have been other variables not taken into consideration.

Chestnut et al,[15] in 1987, showed in a blinded study that using a continuous infusion of 0.75% lidocaine beyond a cervical dilatation of 8 cm did not prolong the second stage or increase the incidence of instrumental deliveries in nulliparous patients. However, it did not provide adequate analgesia or perineal anesthesia.

In a subsequent study, Chestnut et al,[16] in 1987, demonstrated an increase in the second stage of labor (124 versus 94 minutes) and an increase in the use of instrumental delivery, both forceps and vacuum (53 versus 28%) in nulliparous women in whom epidural analgesia was maintained with 0.125% bupivacaine compared with a group whose analgesia was allowed to wear off. However, maintenance of the anesthesia did not increase the incidence of cesarean sections or abnormal presentations of the vertex. There were no deleterious effects on the fetus caused by maintaining analgesia. There were no significant differences between groups in umbilical cord acid-base values and Apgar scores.[16]

Most recently, (1988) Chestnut et al[17] compared 0.125% bupivacaine with 0.0625% bupivacaine with fentanyl 2 μg per mL and showed that both prolonged the second stage of labor, and there was equal use of instrumental deliveries and analgesia.

Abboud et al[3] evaluated the use of continuous infusion epidural analgesia in parturients, both primiparas and multiparas, receiving 0.125% bupivacaine at a rate of 14 mL per hour, 0.75% chloroprocaine at 27 mL per hour, and 0.75% lidocaine at a rate of 14 mL per hour. There was no difference in the duration of the first stage or uterine activity among the three groups but the bupivacaine group had a significantly longer second stage (171 versus 113 minutes for the chloroprocaine group and 67 minutes for the lidocaine group). However, the analgesia was allowed to wear off if the patients lacked the urge to push. The number of instrumental deliveries and cesarean sections was significantly higher in the bupivacaine group compared with the other two groups. There was also a significantly higher incidence of late and variable fetal heart rate changes in the bupivacaine group compared with the other groups. These decelerations occurred between 5 minutes and 4.5 hours after the induction of epidural anesthesia. There was no difference in the 1- and 5-minute Apgar scores (6 or lower) and the Neurologic and Adaptive Capacity Score among the three groups. The umbilical artery and vein acid-base values were within normal limits for all groups.[3]

Bates[9] found that uterine activity integrals in the second stage of labor in parturients with epidurals was significantly lower than those without epidural analgesia.

Livnat et al[42] studied the acid-base status of neonates delivered either spontaneously or by low forceps or vacuum extraction. There was no difference in pH and base deficit of infants born by instrumental versus spontaneous delivery if the duration of the second stage was less than 30 minutes.[42] Therefore, instrumental delivery is not detrimental to the acid-base status of the newborn.

Kaminski et al[37] published a retrospective review of 155 patients who had received 0.25% bupivacaine 10 mL and top-off doses of the same amount when needed. The frequency of instrumental deliveries was 50 versus 20% for a control group. The limitation of this study is that it is retrospective. Bailey and Howard[7] showed there was a decrease in spontaneous deliveries in the first 2 years after the initiation of an epidural service but there was no difference in instrumental deliveries in a subsequent year. They attributed this initial increase in instrumental deliveries to "midwive's distress."[7]

Factors that are thought to contribute to the use of forceps include relaxation of pelvic floor musculature and a delay in the rotation of the fetal head by decreasing the bearing down reflex (the efficacy of pushing may be reduced); the block of Ferguson's reflex (parasympathetic nerves), which causes an oxytocin surge; and fluid loading, which depresses antidiuretic hormone and oxytocin release. Goodfellow et al[26] measured plasma oxytocin levels in patients with epidurals and in a group without epidurals. There was a significant increase in oxytocin in the patients without epidurals between full dilatation and crowning. They concluded that the need for forceps associated with epidurals might be reduced by giving exogenous oxytocin.

Because there does not seem to be any detrimental effects on the neonate with a longer second stage or with proper application of instruments for outlet vaginal delivery, epidural analgesia should be continued through the second stage whenever possible. The concentration and volume of the local anesthetic may be adjusted to maximize the patient's motor strength while maintaining good pain relief. It is very undesirable to the patient to allow the analgesia to wear off. If a parturient is properly instructed she can and will push adequately under epidural analgesia and she does not need pain to prod her into bearing down.

In 1988, the American College of Obstetricians and Gynecologists issued a recommendation that a forceps delivery be considered in nulliparous patients receiving an epidural anesthetic whose second stage of labor is greater than 3 hours, or more than 2 hours in a patient not receiving a regional anesthetic. This statement encourages physicians to be more patient and give the patients with epidural blockade a chance to have a vaginal delivery.[47]

In summary, epidural anesthesia does not significantly affect uterine activity during the first stage of labor. There may be a transient decrease in uterine activity that is most likely related to maternal hypotension, aortocaval compression, systemic absorption of larger than normal doses of local anesthetics, the inhibition of oxytocin by fluid loading, or the absorption of epinephrine from epinephrine-containing solutions. In more recent controlled studies it appears that when pain is adequately relieved, the duration of the second stage is increased. An increased duration of the second stage is not a problem as long as the fetus is continuously monitored and the fetal heart tracing and acid-base status is normal. There are conflicting reports regarding the use of instrumental deliveries in patients with epidural blocks. The bulk of the literature suggests that there is a higher incidence of forceps and vacuum deliveries in those patients receiving epidural anesthesia through the second stage, whereas other data show no difference. Some of the confusion may be due to the variability of the methods in the various studies.

LUMBAR EPIDURAL ANESTHESIA

Prior to the initiation of epidural anesthesia in the parturient it is necessary to evaluate the fetal heart tracing. Before inducing a block, we as anesthesiologists should be aware of the fetal status. Any worrisome pattern should be discussed with the obstetrician and further evaluated with a fetal scalp sample as indicated.

Epidural blocks are induced when the cervix is 3 to 4 cm dilated in the primiparous patient and 3 cm in the multipara. Labor should be in the active phase and will not be slowed down by neural blockade.

Since the parturient is at risk for aspiration of gastric contents some anesthesiologists administer a nonparticulate antacid to raise the gastric pH as prophylaxis in case an untoward event that may compromise the protective airway reflexes during the initiation of the block occurs.

All precautions to avoid hypotension need to be taken. A 1 L solution of Ringer's lactate is given within 20 minutes of the initiation of the block. Exceptions to this acute hydration are patients with severe preeclampsia, the patient receiving beta agonists, and any other medical condition that predisposes the patient to pulmonary edema.

Either the sitting or lateral position is satisfactory. The L2 to L3 or L3 to L4 interspace is usually chosen, but if the interspace is narrow or difficult to palpate then another interspace is appropriate. The epidural is performed in the usual manner.

USE OF A CARDIOVASCULAR MARKER AND TEST DOSE

Perforation of an epidural vein by a needle or catheter in the gravid parturient occurs in nearly 3% of the patients in some series.[22]

Entry into a vein is not always obvious, whereas that of a dural puncture is usually readily detected. In the nonpregnant population, an intravascular injection of 15 μg of epinephrine reliably produced a tachycardia lasting at least 30 seconds.[45] The usefulness of an epinephrine-containing test dose is controversial in the laboring patient. The patient is usually tachycardic to start with and many times does not have continuous ECG monitoring, so the reliability of an intravascular injection of epinephrine is questionable.[40] Systemically absorbed epinephrine may have deleterious effects on the fetus by decreasing uterine blood flow.[59] Systemically injected epinephrine may be especially dangerous in the preeclamptic patient who could then become severely hypertensive.

Proponents of an epinephrine test dose argue that the decrease in uterine blood flow would be transient, as seen in animal studies. Also, the morbidity related to an intravascular injection of a large dose of local anesthetic is much greater than that of the epinephrine.

A test dose of isoproterenol may be a safer alternative to epinephrine in the laboring parturient. Isoproterenol 0.005 mg consistently produced an increase in maternal heart rate of at least 30% in gravid ewes and did not decrease uterine blood flow.[8] Chloroprocaine, 100 mg, given intravenously in male volunteers has been shown to be 100% sensitive and specific for producing symptoms.[28]

There is no agreed upon test dose for the laboring patient. To avoid disastrous complications, it is best to aspirate prior to each injection, give every dose as if it were a test dose utilizing 3- to 5-mL increments and allowing a sufficient amount of time to detect a subarachnoid or intravascular injection. Slowly inject the anesthetic and have resuscitation equipment immediately available. The best monitor is the patient, therefore frequently observe and ask for evidence of intravenous injection.

THE DIFFICULT BACK

Some anesthesiologists consider lumbar epidural anesthesia to be contraindicated in patients with previous spinal surgery. Case reports of epidural anesthesia in patients with extensive spinal surgery for idiopathic kyphoscoliosis shows that it can be safe and effective.[24] The insertion of the needle through the midline or lateral approach in the fused area may not be possible because of the presence of scar tissue or bone. Success in reaching the epidural space requires palpating for an intervertebral space below the fusion and proceeding in the usual fashion. If the fusion extends to S1, attempts need to be made at various interspaces. There may be many false passages and no anesthesia will develop. However, the epidural space may be reached because of a defect in the fusion. In 12 obstetric patients with Harrington rods extending from T4 to L5 to S1, the epidural space was reached in six patients. There was a dural puncture in one of the six. In the five patients with successful epidurals, the local anesthetic requirement was the same as in patients without spinal surgery. None of the patients developed back pain.[31]

CHOICE OF LOCAL ANESTHETICS

There are essentially three local anesthetics of various concentrations that are commonly used and numerous combinations of local anesthetics and opioids with and without epinephrine that are safe and provide excellent analgesia. The needs of the pregnant patient and her obstetrician can best be met by the use of various concentrations and volumes of local anesthetics in combination with opioids.

Local anesthetics differ in their onset time, duration, intensity of sensory and motor block, toxicity, predisposition to the development of tachyphylaxis, and effects on the neonate. Other factors are the concentration, volume, and the addition of epinephrine and opioids.

Chloroprocaine has a very rapid onset and a short duration of action, 45 to 60 minutes. Its systemic toxicity is the lowest because of its ultra-short half-life of 21 seconds in the mother and 43 seconds in the fetus. Because of this short half-life, chloroprocaine has the unique property of no cumulative toxicity. It is often the drug of choice when converting a labor epidural to one for a cesarean section in the case of fetal distress. There was an association of permanent neurologic injury as well as adhesive arachnoiditis and unintentional subarachnoid injection of a large volume of chloroprocaine. This is thought to be due to the combination of the low pH of the solution and the presence of the antioxidant sodium bisulfite. There is currently available a bisulfite-free chloroprocaine. Methyl and propyl-paraben are preservatives added to local anesthetics. These compounds are known to cause severe and intractable contract dermatitis. In the United States and Canada, it has been recommended for many years that these preservatives should not be employed for caudal or epidural anesthesia.[54]

Lidocaine with epinephrine is rapid in onset, reliable, and has an intermediate duration of action, 70 to 90 minutes. It is suited for a top-up dose for perineal anesthesia, short duration multigravida labors, and for cesarean sections. Tachyphylaxis may develop after four or five top-up doses. An acidotic fetus will ion-trap the lidocaine, which may result in further depression, especially in premature fetuses.

Bupivacaine is the most commonly used drug for labor. It has a slow onset and a longer duration of action, 2 to 3 hours. It is indicated for long labors or for use in early labor. Its effectiveness is increased by the addition of opioids and epinephrine. Motor block is more common when using the 0.5% concentration. Bupivacaine 0.75% is no longer recommended for use in obstetrics because of cardiotoxicity and related maternal mortality.[6] Although the 0.75% concentration per se is not more cardiotoxic, it is possible for the anesthesiologist to administer more milligrams more rapidly with this solution.

CONTINUOUS INFUSION EPIDURALS

Continuous infusion lumbar epidurals have become increasingly popular and are used exclusively at many centers. The advantages are (1) the provision of constant analgesia; (2) the maintenance of a more stable maternal cardiovascular system; (3) if the catheter migrates into a vein, the block will dissipate but there will be no local anesthetic toxicity; and (4) if there is migration into the subarachnoid space, the block will rise slowly. The disadvantages are that the rate of the infusion may not be satisfactory and intermittent bolus injections may be necessary to maintain adequate analgesia, and that motor block is not uncommon after a few hours. The rate of the infusion may be adjusted up or down depending on the density and level of the block. The use of continuous infusion epidural analgesia does not decrease the amount of attention the anesthesiologist needs to give the patient. These patients need to be evaluated at regular intervals to assess the levels of the sensory and motor blocks and require continuous fetal heart rate monitoring.

Bupivacaine 0.125% (with or without an opioid and epinephrine) at a rate of 10 to 14 mL per hour is a popular method of managing a continuous infusion for the first stage of labor. The patient is comfortable but retains some sensation, and there is less of a motor block than with higher concentrations. There is a higher incidence of top-up doses compared with 0.25% bupivacaine, but it seems to be a reasonable compromise.

EPIDURAL USE OF OPIOIDS

The rationale for the combination of opioid and local anesthetic is that more dilute solutions of the local can be used, thereby decreasing the amount of motor block and enabling the parturient to push more effectively. Justins showed, in 1982, that the addition of fentanyl 80 μg to a test dose of 0.5% bupivacaine had a more rapid onset, more prolonged, and more complete analgesia than that produced by the same dose of bupivacaine alone.[36] The addition of fentanyl improves the analgesic quality of the dilute concentrations of 0.125% bupivacaine.[60] Cohen et al,[19] evaluated the addition of fentanyl 50 and 100 μg to 0.25% bupivacaine 9 mL. They showed no significant improvement in analgesia compared with that produced by bupivacaine alone. It is concluded that the addition of fentanyl improves the analgesia when added to dilute solutions of local anesthetics or small volumes of more concentrated solutions. The mass (mg) of bupivacaine needed for adequate analgesia is reduced.

The addition of sufentanil, 20 μg, to 0.25% bupivacaine increased the duration of analgesia by over 50%. Sufentanil, 30 μg, caused a more rapid onset than bupivacaine alone. Although the duration was prolonged and onset more rapid with sufentanil, the quality of anesthesia was similar to 0.25% bupivacaine.[48] A potential disadvantage to using sufentanil is that the required doses are relatively large and if injected intravenously could result in respiratory depression.

Abboud et al, studied the effects on the duration of analgesia, the lengths of the first and second stages, and the side effects of butorphanol, 1 to 2 mg, and morphine, 2 mg, to bupivacaine 0.25%. They found the duration of analgesia to be 40% longer for the butorphanol groups and 100% longer for the morphine group when compared with the bupivacaine 0.25% control group. The duration of the first and second stages was not significantly different. The side effects, pruritis and somnolence, occurred only in the morphine group. All neonates were vigorous and had good Apgar scores, acid-base values, and neurobehavioral adaptive capacity scores (NACS).[5]

Occasionally, the patient receiving fentanyl will complain of pruritis. In most cases, this does not require treatment. Naloxone or nalbuphine in small doses relieves the itching without decreasing the analgesia.

The continuous infusion at a rate of 10 mL per hour of alfentanil, 10 μg per mL, and bupivacaine 0.125% had a faster onset and provided better analgesia than bupivacaine 0.25% at the same rate. The total bupivacaine doses were 61 mg in the alfentanil group and 114 mg in the control group.[14]

Epidural opioids alone are usually insufficient for the relief of pain for labor and delivery. Epidural morphine, 7.5 mg, did not relieve stage one or two pain,[32] but subarachnoid morphine and fentanyl have been effective.[41] This combination may be useful in the patient who has cardiac disease and would not tolerate a decrease in systemic vascular resistance produced by the sympathectomy associated with epidural local anesthetics.

In summary, the addition of an opiate to a local anesthetic augments the analgesia, produces a faster onset, and prolongs the duration.[14, 36, 48, 58, 60]

ADDITION OF EPINEPHRINE TO LOCAL ANESTHETICS

The addition of epinephrine is controversial. Epinephrine has not been shown to improve analgesia of a dilute solution of local anesthetic, 0.125% bupivacaine, and an opioid, fentanyl 1 μg per mL, but epinephrine did increase the incidence of profound motor block.[43] However, others have shown it will intensify the quality of the bupivacaine and fentanyl effect.[60] Its use in higher concentrations of local anesthetics augments the motor blockade and is not desirable. Table 3 summarizes the loading and continuous infusion doses of local anesthetics and opioids currently used for labor.

After initiating the block with the loading solution, assure that it is working properly and is bilateral. If it is not effective, insert another catheter. If it seems patchy administer another 3 to 5 mL of the loading solution or readjust the catheter, that is, pull back 1 cm. Once an effective block is established, begin the infusion. If there is break-

Table 3. *Loading and Continuous Infusion Doses of Local Anesthetics and Opioids Used for Labor*

DRUG	LOADING SOLUTION	INFUSION SOLUTION	RATE (ML/HR)
Bupivacaine (B)	8–10 mL of 0.25%	0.25% B	7
	As above	0.125% B	12–14
	As above plus fentanyl 50 μg	0.125% B and fentanyl 2 μg/mL	10–12
	10 mL of infusion solution	0.125% and sufentanil 1–2 μg/mL	10–12
	0.125% B and alfentanil 10 μg/kg 10 mL	0.125% B and alfentanil 10 μg/mL	10
	0.125% B, fentanyl 50–100 μg, epinephrine 1:400,000 10 mL	10 mL bolus of loading solution	As needed
Lidocaine (L)	1% L 9 mL, fentanyl 50 μg, epinephrine 1:400,000	0.75% L fentanyl 2 μg/mL	10
Chloroprocaine	2% Nesacaine methyl paraben free 10 mL	0.5% Nesacaine methyl paraben free	30

through pain, a bolus of 5 to 10 mL of the loading solution and an increase in the infusion rate or an increase in the concentration of the infusion solution may prove helpful.

If the block wears off or does not improve, the catheter may have migrated into a vein or out of the epidural space. It is important to emphasize that every bolus given through the catheter needs to be a 3 to 5 mL test dose because of the possibility of this migration.

The catheter may migrate into the subarachnoid or subdural space. The infusion of weak solutions of local anesthetics will cause a high block in 20 to 30 minutes, usually with a marked motor block of the lower extremities.[29] (High block is discussed later in this article.) It is important to instruct the patient to notify the nurse if she cannot move her legs. A member of the anesthesia team will be called by the nurse to evaluate the patient.

EFFECTS ON FETUS

As mentioned previously, there is improvement in the acid-base status in those neonates whose mother received epidural analgesia. Better control of delivery reduces risks of trauma to the infant. Some hazards include a decrease in uterine blood flow caused by maternal hypotension. The use of bupivacaine was associated with a greater amount of fetal heart rate abnormalities as compared with chloroprocaine and lidocaine, but there was no difference in outcome.[1, 2] The addition of opioids has been shown to have no effect on Apgar scores, acid-base status, and NACS.

COMPLICATIONS

Crawford reviewed 26,490 consecutive cases of labor epidurals. There were nine potentially life-threatening events that were either unintentional subarachnoid or intravenous injections of local anesthetics. There were two serious but not life-threatening problems; one was an epidural abscess caused by an unsuspected vaginal streptococcal infection and the other was the development of a localized fibrotic reaction from a spicule of foreign material introduced into the epidural space that necessitated laminectomy. Thirteen were moderately serious including hypotension, severe hypertension, hyperalgesia (unexplained), leg pain, numbness, weakness, and backache. There were 17 mildly disturbing incidents that were primarily shearing off of a small part of the catheter in the epidural space. None of these complications resulted in permanent injury, with the exception of two laminectomy scars.[21]

Hypotension

Hypotension is one of the more common complications. It is usually caused by inadequate intravenous fluid preload or aortocaval compression. A high block caused by an unintentional subarachnoid or subdural injection or a massive epidural is fortunately less common but a more severe problem that necessitates airway control as well as treatment of the hypotension. The etiology, prevention, and treatment have been discussed previously in this text.

Seizures

Seizures are the result of accidental intravascular injections. Securing the airway is the first step to be taken, because all parturients are at risk for aspiration. These seizures are self-limiting and usually do not last more than a few minutes. Giving the local anesthetic in 5-ml increments protects against achieving high plasma levels of drug in the case of the epidural needle or catheter being in an epidural vein. Patients may unreliably experience tinnitus, a metallic taste, dizziness, or other signs of mild central nervous system toxicity with these smaller doses. If a patient is not achieving a level or if the level has worn off (in the case of a continuous infusion), consider intravenous migration of the catheter.

Dural Puncture

The incidence of dural puncture varies with the experience of the anesthetist. Overall, there is an incidence of 2 to 3%.[22] The incidence of headache can be greater than 70% with an 18-gauge needle.[13] Headache develops within 48 hours and is usually more severe on the second day. Repeating the epidural at another interspace and cautiously administering the local anesthetic is recommended. Some of the drug may enter the CSF via the puncture, so it is important to give small boluses and reassess after each increment.

Although older information has suggested lack of effectiveness, 15 to 20 mL of autologous blood given through the catheter after delivery may avoid the development of a headache. A recent study evaluated the effectiveness of immediate prophylactic blood patching. Fifteen to 20 mL of autologous blood was given through the catheter in 10 nonobstetric patients and was effective in 100% of the cases.[51]

High Block

A potentially life-threatening problem is that of a high block. This may be caused by subdural or subarachnoid migration of the catheter or by massive epidural spread. Turning the epidural needle once it is in the epidural space may lacerate a section of the dura and predispose one to a subdural or subarachnoid injection. The first complaint by the patient may be dyspnea and if the high block is not recognized and treated immediately she may progress to respiratory and cardiovascular arrest. The patient may not be under close supervision when the catheter has migrated through the dura and therefore poses a more dangerous situation than if it occurs soon after placement of the epidural. Failure to aspirate cerebrospinal fluid from the catheter does not rule out subarachnoid placement.

A subdural migration or placement of a catheter is the insertion of the catheter between the dura and arachnoid membranes. The characteristics of the block are moderate hypotension, slow onset of symptoms (15 to 20 minutes), slow onset of respiratory distress, and complete recovery in about 2 hours. The only way to confirm a subdural placement is by the injection of contrast material via the catheter into the subdural space. The radiographic appearance is characteristic.

Inadequate Block

Occasionally analgesia is incomplete over a localized area or is unilateral. Unblocked segments have been reported to occur in about 15% and unilateral blocks in 1.3% of lumbar epidurals.[20] In most cases there is a technical explanation and the problem is readily remedied. If one or more spinal segments are not blocked, the addition of 5 mL of the local anesthetic solution, with the patient in the complete lateral position with the affected side down, usually solves the problem. The addition of an opioid is often beneficial in this situation. In rare cases, the pain persists in spite of additional local anesthetic and opioid, and replacing the catheter may help. This problem of "patchy" block remains an enigma.

Unilateral blocks occur with catheter placement in the anterior area (ventral) of the nerve roots.[57] If the block is not completely unilateral, the addition of more local may help, but a completely unilateral block usually requires pulling back the catheter 1 cm or repeating the epidural. It is recommended to not thread the catheter more than 3 cm beyond the tip of the needle because it is more likely to pass out of the epidural space through the intervertebral foramen or kink or knot in the epidural space.

It is usually futile and potentially dangerous to give repeated injections when the block is unsatisfactory. It is best to replace the catheter at another space after one or two unsuccessful boluses.

Backache

The incidence of low back pain has been reported to be 30 to 40% following delivery.[20] Back pain is not caused by epidural anesthesia but is caused by not supporting the lordotic curve of the lumbar area during labor and delivery.

Other Neurologic Problems

Adhesive arachnoiditis was mentioned earlier in the text and is an infrequent problem. With the newer bisulfite-free chloroprocaine and methyl-paraben–free (MPF) local anesthetics, its incidence should be extremely low.

Most nerve deficit problems are due to labor and delivery and not due to the use of epidural anesthesia. Foot drop results from compression of the lateral popliteal (common peroneal) nerve at the level of the neck of the fibula by a stirrup. A prolonged lithotomy position can cause compression of the lateral femoral cutaneous nerve at the inguinal ligament and result in decreased sensation over the lateral thigh. Sciatica may be caused by sciatic nerve compression by the fetal head or forceps. It is important that the anesthesiologist investigate any neurologic complaint and involve a neurologist. An electromyogram performed early and some weeks later can help determine the location and time of occurrence of the injury.

An epidural abscess and hematoma are extremely rare. If a patient is receiving mini-dose heparin, obtain a partial thromboplastin time before proceeding with an epidural. Preeclamptics may have normal platelet counts but dysfunctional activity.[52] Currently there is no universally agreed upon recommendation about doing a bleeding time on these patients. If a patient has a recrudescence of herpes simplex II, there is no viremia and it is appropriate to administer an epidural as long as there are no cutaneous lesions in the lumbar area. Obviously, an epidural should not be placed if there is a coagulopathy or untreated infection. If the anesthesiologist suspects cord compression by a lesion, it is crucial to have a neurologist evaluate the patient immediately.

Unrecognized Uterine Rupture

The cesarean section rate in the United States is 24%. More women are being strongly encouraged to have vaginal births after cesarean sections. A trial of labor is successful in 50 to 80% of women with previous low transverse uterine incisions. There is no report of a maternal death due to the rupture of this type of incision. However, a concern has been that epidural analgesia may mask the pain of rupture. Crawford has suggested that pain of organ rupture will break through routine epidural analgesia. Furthermore, pain and uterine tenderness are not sensitive indicators of a lower uterine scar dehiscence. Epidural anesthesia has not been found to have adverse effects on the patient undergoing a vaginal birth after cesarean section.[53] These patients should all have a fetal monitor and uterine activity monitor in situ.

SUMMARY

Epidural anesthesia for labor and delivery is the safest technique that provides complete pain relief. The discovery of spinal opiate receptors and the effectiveness of small doses of opiates augmenting the analgesia of dilute concentrations of local anesthetics has greatly increased the choice of solutions in the anesthesiologist's armamentarium. We are better able to customize the anesthetic to the needs of the patients and our obstetric colleagues. The benefits of epidural anesthesia are numerous and the risks small when proper precautions are taken.

REFERENCES

1. Abboud TK, Khoo SS, Miller F, et al: Maternal, fetal, and neonatal responses after epidural anesthesia with bupivacaine, 2-chloroprocaine, or lidocaine. Anesthesiology 62:638–644, 1982
2. Abboud TK, Artal R, Henrikson EH, et al: Effects of spinal anesthesia on maternal circulating catecholamines. Am J Obstet Gynecol 142:252, 1982
3. Abboud TK, Afrasiabi A, Sarkis F, et al: Continuous infusion epidural analgesia in parturients receiving bupivacaine, chloroprocaine, or lidocaine—maternal, fetal, and neonatal effects. Anesth Analg 63:421–428, 1984
4. Abboud TK, Sheik-ol-Eslam A, Yanagi T, et al: Safety and efficacy of epinephrine added to bupivacaine for lumbar epidural analgesia in obstetrics. Anesth Analg 64:585–591, 1985
5. Abboud TK, Afrasiabi A, Zhu J, et al: Epidural morphine or butorphanol augments bupivacaine analgesia during labor. Anesthesiology 69:A684, 1988
6. Albright G: Anesthesia in Obstetrics; Maternal, Fetal and Neonatal Aspects. Menlo Park, CA, Addison-Wesley, 1978
7. Bailey PW, Howard FA: Epidural analgesia and forceps delivery: Laying a bogey. Anaesthesia 38:282–285, 1983
8. Baker BW, Longmire S, Jones MM, et al: The epidural test dose reconsidered. Anesthesiology 67:A625, 1987
9. Bates RG, Duncan A, Edmonds DK: Uterine activity in the second stage of labour and the effect of epidural analgesia. Br J Obstet Gynecol 92:1246–1250, 1985
10. Bonica JJ: Principles and Practice of Obstetric Analgesia and Anesthesia. Oxford, Blackwell, 1967
11. Bonica JJ: Peripheral mechanism and pathways of parturition pain. Br J Anaesth 51:38, 1979
12. Bromage PR: Epidural Analgesia. Philadelphia, W.B. Saunders, 1978, pp 513–600
13. Brownridge P: The management of headache following accidental dural puncture in obstetric patients. Anesth Intens Care 11:4–15, 1983
14. Carp H, Johnson MD, Bader AM, et al: Continuous epidural infusion of alfentanil and bupivacaine for labor and delivery. Anesthesiology 69:A687, 1988
15. Chestnut DH, Bates JN, Choi WW: Continuous infusion epidural analgesia with lidocaine: Efficacy and influence during the second stage of labor. Obstet Gynecol 69:323–327, 1987
16. Chestnut DH, Vandewalker GE, Owen CL, et al: The influence of continuous ep-

idural bupivacaine analgesia on the second stage of labor and method of delivery in nulliparous women. Anesthesiology 66:774–780, 1987
17. Chestnut DH, Owen CL, Bates JN, et al: Continuous infusion epidural analgesia during labor: A randomized, double-blind comparison of 0.0625% bupivacaine/ 0.0002% fentanyl versus 0.125% bupivacaine. Anesthesiology 68:754–759, 1988
18. Cibils LA: Response of human uterine arteries to local anesthetics. Am J Obstet Gynecol 126:202–210, 1976
19. Cohen SE, Tan S, Albright GA, et al: Epidural fentanyl/bupivacaine mixtures for obstetric analgesia. Anesthesiology 67:403–407, 1987
20. Crawford JS: The second thousand epidural blocks in an obstetric hospital practice. Br J Anaesth 44:1277–1287, 1972
21. Crawford JS: Some maternal complications of epidural analgesia for labour. Anaesthesia 40:1219–1225, 1985
22. Dawkins CJM: Analysis of the complication of extradural and caudal block. Anaesthesia 24:554–563, 1969
23. Deckardt R, Fembacher PM, Schneider KT, et al: Maternal arterial oxygen saturation during labor and delivery: Pain-dependent alterations and effects on the newborn. Obstet Gynecol 70:21–25, 1987
24. Feldstein G, Ramanathan S: Obstetrical lumbar epidural anesthesia in patients with previous posterior spinal fusion for kyphoscoliosis. Anesth Analg 64:83–85, 1985
25. Gibbs CP, Krischer J, Peckham BM, et al: Obstetric anesthesia: A national survey. Anesthesiology 65:298–306, 1986
26. Goodfellow CF, Hull MGR, Swaab DF, et al: Oxytocin deficiency at delivery with epidural analgesia. Br J Obstet Gynecol 90:214–219, 1983
27. Greiss FC, Still JG, Anderson SG: Effects of local anesthetic agents on uterine vascular tone and myometrium. Am J Obstet Gynecol 124:889, 1976
28. Grice SC, Eisenach JC, Dewan DM, et al: Evaluation of 2-chloroprocaine as an effective intravenous test dose for epidural analgesia. Anesthesiology 67:A627, 1987
29. Hanson AL, Hanson B: Continuous mini-infusion of bupivacaine in the epidural space during labor. Experience from 1000 deliveries. Reg Anesth 10:139–144, 1985
30. Hollmen A, Jouppila R, Jouppila P, et al: Effect of extradural analgesia using bupivacaine and 2-chloroprocaine on intervillous blood flow during normal labour. Br J Anaesth 54:837–842, 1982
31. Hubbert CH: Epidural anesthesia in patients with spinal fusion. Anesth Analg 64:843, 1985
32. Hughes SC, Rosen MA, Shnider SM, et al: Maternal and neonatal effects of epidural morphine for labor and delivery. Anesth Analg 63:319–324, 1984
33. Jouppila R, Jouppila P, Hollmen A, et al: Effect of segmental extradural analgesia on placental blood flow during normal labour. Br J Anaesth 50:563–567, 1978
34. Jouppila R, Jouppila P, Karinen JM, et al: Segmental epidural analgesia in labour: Related to the progress of labour, fetal malpostion and instrumental delivery. Acta Obstet Gynecol Scand 58:135–139, 1979
35. Jouppila P, Jouppila R, Hollmen A, et al: Lumbar epidural analgesia to improve intervillous blood flow during labor in severe preeclampsia. Obstet Gynecol 59:158–161, 1982
36. Justins DM, Francis D, Houlton PG, et al: A controlled trial of extradural fentanyl in labour. Br J Anaesth 54:409, 1982
37. Kaminski HM, Stafl A, Aiman J: The effect of epidural analgesia on the frequency of instrumental obstetric delivery. Obstet Gynecol 69:770–773, 1987
38. Lederman RP, McCann DS, Work B, et al: Endogenous plasma epinephrine and norepinephrine in last-trimester pregnancy and labor. Am J Obstet Gynecol 129:5, 1977
39. Lederman RP, Lederman E, Work BA, et al: The relationship of maternal anxiety, plasma catecholamines, and plasma cortisol to progress in labor. Am J Obstet Gynecol 132:495, 1978
40. Leighton BD, Norris MC, Sosis M, et al: Limitations of an epinephrine epidural anesthesia test dose in laboring patients. Anesthesiology 66:688–691, 1987

41. Leighton BL, DeSimone CA, Norris MC, et al: Intrathecal narcotics for labor revisited: Fentanyl 25 μg and morphine 0.25 mg provide rapid, profound analgesia. Anesthesiology 69:A680, 1988
42. Livnat EJ, Fejgin M, Scommegna A, et al: Neonatal acid-base balance in spontaneous and instrumental vaginal deliveries. Obstet Gynecol 52:549–551, 1978
43. Lysak SZ, Eisenach JC, Dobson CE: Patient controlled epidural analgesia (PCEA) during labor: A comparison of three solutions with continuous epidural infusion (CEI) control. Anesthesiology 69:A690, 1988
44. Moir DD, Thorburn J: Obstetric Anaesthesia and Analgesia, ed 3. London, Bailliere Tindall, 1986, pp 272–275
45. Moore DC, Batra MS: The components of an effective test dose prior to epidural block. Anesthesiology 55:693–696, 1981
46. Naulty JS, Smith R, Ross R: Effect of changes in labor and analgesic practice on labor outcome. Anesthesiology 69:A660, 1988
47. Obstetric forceps. American College of Obstetricians and Gynecologists Committee Opinion #59. February 1988
48. Phillips G: Epidural sufentanil/bupivacaine combinations for analgesia during labor: Effect of varying sufentanil doses. Anesthesiology 67:835–838, 1987
49. Phillips JC, Hochberg CJ, Petrakis JK, et al: Epidural analgesia and its effects on the "normal" progress of labor. Am J Obstet Gynecol 129:316–323, 1977
50. Phillips KC, Thomas TA: Second stage of labour with or without extradural analgesia. Anaesthesia 38:972–976, 1983
51. Quaynor H, Corbey M: Extradural blood patch, why delay? Br J Anaesth 57: 538–540, 1985
52. Ramanathan J, Sibai BM, Vu T, et al: Correlation between bleeding times and platelet counts in preeclamptic women undergoing cesarean section. Anesthesiology 69:A694, 1988
53. Rudnick V, Niv D, Hetman-peri M, et al: Epidural analgesia for planned vaginal delivery following previous cesarean section. Obstet Gynecol 64:621–623, 1984
54. Sghirlanzoni A, Marazzi R, Pareyson D, et al: Epidural anesthesia and spinal arachnoiditis. Anaesthesia 44:317–321, 1989
55. Shnider AM, Wright RG, Levinson G, et al: Uterine blood flow and plasma norepinephrine changes during maternal stress in the pregnant ewe. Anesthesiology 50:524–527, 1979
56. Shnider AM, Abboud TK, Artal R, et al: Maternal catecholamines decrease during labor after lumbar epidural anesthesia. Am J Obstet Gynecol 147:13–15, 1983
57. Usubiaga JE, Dos Reis AJ, Usubiaga LE: Epidural misplacement of catheters and mechanisms of unilateral blockade. Anesthesiology 32:159–161, 1970
58. Van Steenberge A: Choice of local anesthetic agents for obstetric purposes. Eur J Obstet Gynecol Reprod Biol 15:355, 1983
59. Wallis KL, Shnider SM, Hicks JS, et al: Epidural anesthesia in the normotensive pregnant ewe: Effects on uterine blood flow and fetal acid-base status. Anesthesiology 44:481–487, 1976
60. Youngstrom P, Eastwood D, patel H, et al: Epidural fentanyl and bupiviacaine in labor: Double-blind study. Anesthesiology 62:A414, 1984

Address reprint requests to

Mary Jo A. Curran, MD
Department of Anesthesiology
Michael Reese Hospital and Medical Center
31st at Lakeshore Drive
Chicago, IL 60616

Obstetric Anesthesia 0889–8537/90 $0.00 + .20

Anesthesia for Cesarean Section

*Laurence S. Reisner, MD**

The anesthetic care of the cesarean section patient has improved dramatically over the last few decades. An interesting and important theme has been that of a shift in emphasis of concern between mother and fetus. During the 1970s the primary focus of both clinical care and academic study was on the effects of anesthetic techniques on the fetus. This much needed concentration was redirected toward the mother in the 1980s as evidence of maternal neurotoxicity and cardiotoxicity from popular local anesthetic agents surfaced. In the current era a reasonable balance of concern has been reached and although the same basic anesthetic choices exist, subtle refinements in technique and a more thorough understanding of the physiology and pharmacology involved have led to a safer outcome for both mother and neonate. Indeed, anesthesia as a cause of maternal death is on the decline. This apparent evolution of safety has been ascribed to the more widespread use of regional anesthesia by some[30] and in all probability to the employment of more extensive physiologic monitoring. Regardless of the anesthetic technique selected, there are certain physiologic and pharmacologic principals that must be recognized and properly managed in order to assure optimum conditions for both mother and fetus.

PREMEDICATION

The usual goals of anesthetic premedication are to dry secretions, prevent vagal activity, provide anxiolysis, ensure analgesia for uncomfortable preoperative procedures, and provide a basal analgesic state. Although some of these goals may be met by psychoprophylactic techniques, others require pharmacologic agents. The majority of cesarean section patients do not require sedative or analgesic preme-

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* Professor of Clinical Anesthesiology and Reproductive Medicine, University of California, San Diego; Vice-Chair, Department of Anesthesiology, Director of Obstetric Anesthesia, University of California, San Diego Medical Center, San Diego, California

dication. It is not unreasonable to administer an anticholinergic agent to this population as it will decrease secretions and lessen the chance of a bradycardia from either sympathetic blockade induced by regional anesthesia or from general anesthetic manipulations. Although atropine may cross the placenta and increase fetal heart rate with a reduction in beat-to-beat variability, glycopyrrolate does not readily do so. This is the agent of choice of many obstetric anesthesiologists. Although this class of drugs has effects desirable for the patient facing an anesthetic, they also are recognized as having a negative effect on maternal lower esophageal sphincter tone. In addition, the patient may be disturbed by the characteristic dry mouth. The anticholinergic agent may be given intramuscularly 30 to 60 minutes prior to surgery or intravenously just prior to administering the anesthetic. On rare occasion preoperative sedation for a cesarean section patient may be in order. This is most efficiently accomplished by intravenous titration of a small amount of a benzodiazepine such as diazepam (2 to 5 mg) or midazolam (0.5 to 2 mg) or a short-acting narcotic such as fentanyl. Small doses of these drugs should have minimal depressant effects on the fetus. Some anesthesiologists prefer to administer a small (5 mg) oral dose of diazepam approximately an hour before a scheduled cesarean section. Although tranquilizers, ataractics, barbiturates, and other sedatives may have some potential maternal benefits as a premedicant, they are usually avoided until after delivery of the infant. They offer little to the patient undergoing general anesthesia, and the patient with regional anesthesia can usually be comforted by the anesthesiologist until delivery.

MONITORING TECHNIQUES

Modern technology has provided us with the ability to noninvasively monitor several important maternal physiologic parameters (Table 1). In addition to the routine monitoring of the EKG, pulse, blood pressure, and heart sounds during cesarean section, the use of these devices may improve maternal safety. One such example is the pulse oximeter, once a novelty and now virtually the standard of care. This device uses a transilluminating sensor that is placed over a nailbed or other vascular area. The sensor detects the pulse wave and measures oxyhemoglobin saturation. The pulse rate and the per cent saturation are displayed on the console and an audible signal quickly

Table 1. *Monitoring the Anesthetized Parturient*

1. Oxygen saturation (pulse oximeter)
2. Blood pressure
3. Precordial stethoscope
4. End-tidal carbon dioxide
5. Electrocardiogram

alerts those in the operating room of declining saturation. This device is accurate and rapidly responsive to falls in arterial oxygen saturation and provides a warning far earlier than do the usual clinical signs of hypoxemia. If placed on the parturient's right foot it may also alert to aortic compression if the pulse wave signal is lost. The pulse oximeter should be employed during regional as well as general anesthesia as problems other than those directly related to anesthesia may be detected, for example, amniotic fluid embolism. Although no strict standard exists as yet, it is quite likely that this type of monitoring will become mandatory for all anesthetic procedures in the near future.

Another very useful piece of equipment is the capnograph. The anesthetist will be alerted almost immediately of an esophageal intubation because no carbon dioxide will be measured with attempted ventilation. This alert occurs even before hypoxia ensues. The end-tidal carbon dioxide tension may also be followed during the course of general anesthesia and used to maintain optimum ventilation. Capnography may also be used to monitor respiration during regional anesthesia (with and without sedation) by connecting an intravenous canula to the sampling tube and inserting it into one of the holes in a green oxygen mask. Although the end-tidal CO_2 reading may not be accurate, it will monitor rate of ventilation and alert the anesthetist if the patient's rate is very slow or becomes apneic. This instrument is also becoming a familiar sight in the operating room. Automated blood pressure cuffs are useful because they not only determine the blood pressure at proscribed intervals, but they also allow for alarm functions at high and low pressures and can provide a permanent paper record. All members of the obstetric care team can see the digital display and thus be aware of the patient's status. Although certainly not required for routine cesarean section, the application of Doppler ultrasound to suprasternal probes allows for the noninvasive determination of maternal cardiac output. The ability to obtain this measurement in a rapid fashion may be of major benefit when managing patients with cardiac disease, preeclampsia, or unexpected obstetric complications.

LEFT UTERINE DISPLACEMENT

The requirement for left uterine displacement during the third trimester of pregnancy is well established (Table 2). Obstruction of the inferior vena cava by the gravid uterus compressing this vessel

Table 2. *Left Uterine Displacement*

1. Allows adequate maternal cardiac venous return
2. Avoids hypotension
3. Avoids increased uterine venous tone
4. Avoids aortic and iliac vessel compression
5. Prevents decreases in uteroplacental blood flow

against the bodies of the lumbar vertebrae may result in a decrease in maternal cardiac output and blood pressure in the supine position as a result of venous pooling. This will lead to a decrease in uterine artery perfusion pressure. Obstruction of uterine venous drainage also diminishes the net uterine perfusion pressure. Uteroplacental perfusion may also be compromised by compression of the aorta or the common iliac artery, even if maternal brachial artery blood pressure appears normal. Left uterine displacement becomes even more critical with the administration of regional anesthesia and its attendant sympathetic blockade. A recent study confirms the significant decrease in cardiovascular performance in gravidas moved from the left lateral tilt position to supine with an epidural anesthetic in place.[21] Therefore, all cesarean section patients should have left uterine displacement, which may be easily accomplished with a wedge made of blankets or towels or can even be achieved by a simple gas-powered inflatable device constructed from materials commonly found in the hospital.[10]

ASPIRATION PROPHYLAXIS

The pregnant patient at term is recognized as being at an increased risk for the regurgitation of gastric contents and their aspiration. This spectre has been well emphasized over the last two decades although failure to secure the airway during general anesthesia is becoming an equally serious or greater problem. It is commonly accepted that the parturient has an elevated intra-abdominal pressure and that the normal relationships of the gastrointestinal tract are altered by the enlarged uterus. The smooth muscle relaxing effects of progesterone on intestinal motility are similarly apparent. Gastric emptying is delayed and the lower esophageal sphincter is rendered less competent.[5] Gastric acid production may also be increased during the last trimester of pregnancy. Thus, the parturient can be assumed to have a full stomach regardless of the time of last ingestion and should she vomit or regurgitate, is at risk for aspirating either particulate matter or acid gastric juice into her bronchopulmonary tree. If one accepts the arbitrary current standard of a gastric volume greater than 25 mL and a pH of less than 2.5 as defining the population at greatest risk, approximately 25% of parturients fall into this category (Table 3). The absolute risk of dying from this complication is virtually impossible to determine as complete records are nonexistent, but in England and Wales this is the cause of death in one out of every 5000 to 6000 cesarean section patients.

At first this risk seems obvious only for general anesthetic techniques, but it is also present during regional anesthesia because a high spinal or epidural anesthetic quite effectively reduces the patient's ability to cough and clear the airway. Central nervous system and cardiovascular responses to unintentional intravascular injections of large amounts of local anesthetic agents also put the patient at similar risk. Thus, the approach to preventing the complication of aspiration

Table 3. *Factors Leading to Regurgitation and Aspiration During Pregnancy*

1. Delayed gastric emptying
   A. Anatomic
   B. Hormonal influences
   C. Narcotic analgesia in labor
   D. Anxiety
2. Increased intragastric pressure
   A. Anatomic
   B. Iatrogenic
3. Decreased lower esophageal sphincter tone
   A. Hormonal
   B. Pharmacologic agents
4. Increased gastric acid secretion
   A. Physiologic
   B. Anxiety

pneumonia is multipronged and of course varies with the selected anesthetic technique.

Since acid aspiration produces a clinical picture similar to a chemical burn or acute adult respiratory distress syndrome, elevating the pH of gastric contents is a primary preventive measure. This may be achieved acutely by the administration of 15 to 30 mL of an oral antacid approximately 30 minutes prior to surgery. These have traditionally been of the particulate suspension type; however, more recent evidence suggests that these are also harmful to the lung and current recommendations are for the use of a clear antacid solution such as 0.3 mol per L sodium citrate.[11] Given adequate time, intragastric pH may be raised by employing a histamine H2 receptor antagonist such as cimetidine. This has been proven effective, but cimetidine impairs the hepatic metabolism of drugs such as the benzodiazepines and local anesthetics that may be undesirable in both mother and fetus. Currently ranitidine is being evaluated as it does not appear to interfere as much in this fashion. These drugs are often used in combination with an oral antacid.

While elevating the pH can be successfully accomplished, efforts to decrease the volume of gastric contents are less encouraging. Gastric suction has been advised but cannot be relied on fully to evacuate the stomach and is obviously uncomfortable for the patient. A pharmacologic approach to this problem has been studied with the chlorbenzamide derivative metoclopramide. It is an antiemetic and accelerates gastric emptying by sensitizing gastric smooth muscle to the action of acetylcholine as well as having a direct autonomic effect. It also appears to elevate lower esophageal sphincter tone. Although it has been demonstrated to accelerate gastric emptying in mid-trimester abortion patients, it has not been shown to be as effective in cesarean section patients and its routine use has not been recommended.[6]

Patients undergoing regional anesthesia for cesarean section should have their gastric contents alkalinized. Those undergoing gen-

Table 4. *Measures to Prevent Aspiration with General Anesthesia*

1. Oral antacid prophylaxis
2. Histamine H2 receptor blockage if adequate time
3. Metoclopramide administration (of questionable value)
4. Rapid sequence induction (or awake intubation for difficult airway)
5. Cricoid pressure during induction
6. Cuffed endotracheal tube
7. Extubation when awake and protective reflexes present

eral anesthesia are at greatest risk during the induction and emergence phases. The currently practiced technique is primarily oriented to minimize this maternal risk by employing a rapid sequence induction while an assistant maintains cricoid pressure. A cuffed endotracheal tube is inserted as soon as possible. The tube remains in situ until the patient is awake and has regained her protective reflexes. These steps allow for optimum protection of the airway during the time that the patient has lost her protective reflexes as a result of the induction agents and is most likely to regurgitate. Skillful mechanical protection from regurgitation (cricoid pressure) and protection of the airway (endotracheal tube) are the most important maneuvers in reducing the risk of an aspiration pneumonia associated with general anesthesia (Table 4).

FLUID ADMINISTRATION

The use of adequate volumes of intravenous fluid supplementation has become a well-recognized part of the management of the cesarean section patient. Prior to performing regional anesthesia it is thought to be desirable to infuse between 15 and 30 mL per kg of a balanced salt solution to maintain intravascular volume in face of the sympathetic blockade that is produced. This form of therapy helps to prevent the hypotension that is the result of venodilation and pooling of a major portion of the blood volume in the lower extremities and the splanchnic bed. Although glucose is an essential component of maintenance fluid administration during labor, its use in bolus or resuscitative fluid therapy is probably contraindicated in the obstetric patient. The rapid glucose load leads to a significant elevation in maternal blood glucose level and this is rapidly reflected in the fetal circulation. When the neonate is delivered, and its activity increased, the utilization of glucose is escalated. The insulin response to the prior glucose load is not ablated, however, and hypoglycemia in the second hour of life is likely to occur. Jaundice was also more prevalent in infants of mothers receiving a significant glucose infusion prior to anesthesia for cesarean section.[17] An interesting maternal observation is that colloid osmotic pressure seems to fall significantly in the postpartum period after a crystalloid fluid load.[14] This may be of major concern for patients with preeclampsia or cardiac disease. Fluid loading prior to regional anesthesia is essential and appropriate, but the patient with exceptional circumstances requires additional consideration and monitoring.

Although the availability of blood is essential for the safe conduct of obstetric surgery, the use of the type-and-screen procedure instead of crossmatching two units of whole blood seems far more prudent and cost effective. Studies of blood utilization for cesarean section patients have revealed that only 2 to 3% actually receive blood.[8, 26] The likelihood of a transfusion reaction from type- and Rh-specific blood with a negative antibody screen is virtually the same as after a crossmatch. Blood is rarely needed instantly, so there is time for a crossmatch to be completed in most cases after the blood is requested. Patients at higher risk for requiring transfusion, for example, those who are anemic, who have placenta previa or abruption, a coagulopathy, or severe preeclampsia, are still candidates for a crossmatch prior to cesarean section.

REGIONAL ANESTHESIA

Regional anesthetic techniques are used for at least 60% of cesarean sections nationally and in some institutions this percentage is even greater.[3] This preference for spinal and epidural anesthesia is shared by all involved in the care of the cesarean section patient and her infant as optimum operating conditions with stable hemodynamics and an awake mother may be provided. The father or significant other can be present to reassure the parturient and share in the delights of the delivery. There are, however, some circumstances in which regional anesthesia should be avoided. These would include maternal hypovolemia, coagulopathy, and infection at or near the site of injection. There are several relative contraindications to regional anesthesia that must be weighed on an individual basis. Some have argued that it should be avoided in the presence of severe preeclampsia; however, the use of invasive monitoring and careful fluid and anesthetic management have led many groups to believe that regional anesthesia is quite satisfactory for these patients.[22]

No anesthetic is risk-free and there are complications that attend regional anesthesia for cesarean section. A high or total spinal anesthetic may occur with either spinal or epidural anesthesia. The manifestations include not only complete sensory and motor blockade, but also hypotension, bradycardia, unconsciousness, loss of protective reflexes, and respiratory arrest. As devastating as it appears, prompt intervention by the anesthesiologist to secure the airway with an endotracheal tube and ventilate the patient with oxygen as well as circulatory support with left uterine displacement, raising the legs, and administration of ephedrine should prevent any significant or lasting sequelae. Central nervous system and cardiovascular toxicity may occur if the full epidural dose of local anesthetic is unintentionally

Table 5. *The Epidural Test Dose*

1. Enough local anesthetic to produce spinal anesthesia
2. A tracer (epinephrine) to detect intravenous injection
3. Inject through the final delivery device (catheter or needle)
4. Wait 5 minutes and observe carefully

injected into an epidural vein. Convulsions, unconsciousness, arrhythmias, and cardiovascular collapse may ensue. Treatment is similar to that previously mentioned but more potent cardiac stimulation with drugs such as epinephrine may be required as well as closed-chest cardiac massage and defibrillation. The resuscitation may prove quite lengthy if bupivacaine is the local anesthetic as it produces a profound cardiovascular depression. The pregnant patient appears particularly susceptible to this problem.[23] It is advisable to avoid giving large boluses of drug and to use a test dose designed to alert the anesthetist of probable intravenous placement (Table 5). This is often accomplished by the addition of 15 to 20 μg of epinephrine to the test solution.

The most common side effect of regional anesthesia is hypotension secondary to sympathetic blockade and venous pooling. This is usually not life threatening for the mother but the fetus may be placed at some jeopardy if systolic blood pressure declines more than 25% or falls below 100 mm Hg. Preventive measures include left uterine displacement, intravenous fluid loading just prior to the anesthetic, and occasionally prophylactic ephedrine. These measures reduce the likelihood of hypotension from 85 to about 15%. While ephedrine does cross the placenta, it does not appear to have an adverse effect on the neonate.[15] Therapy is an extension of the preventive measures. Another common concern is the post–lumbar-puncture headache. This may occur after an intentional spinal anesthetic or after an unintentional dura-arachnoid puncture in an attempt at epidural anesthesia. The incidence of headache is greater in the pregnant than in the nonpregnant population and is about 4 to 5% with a 22-gauge spinal needle for cesarean section.[4] The incidence rises with increasing needle size and thus approximates 50% with the 17- to 18-gauge epidural needle. Although this problem can be quite limiting to the post-cesarean section patient, treatment with an epidural blood patch results in significant or complete relief in greater than 90% of patients.

Persistent neurologic deficit is rare after properly conducted regional anesthesia and is estimated to occur in less than 1 in 10,000 anesthetics. An association with a higher frequency of this complication was suggested with 2-chloroprocaine (Nesacaine-CE) particularly when an epidural dose was unintentionally injected into the subarachnoid space. Current research points toward the antioxidant sodium (meta)bisulfite as being the neurotoxin when in a low pH vehicle, although not all groups are in agreement.[13, 24] Recent preparations of the drug have no added bisulfite.

SPINAL ANESTHESIA

Although spinal and epidural anesthesia have many similarities, there are some important, albeit at times subtle differences that may make one more favorable than the other for a given patient. The advantages of spinal anesthesia are numerous. The endpoint of needle placement is clearly indicated by the free flow of cerebrospinal fluid and the time to locate the subarachnoid space usually brief. There is no test dose period to wait through and the onset of anesthesia is rapid. The amount of drug administered is small; therefore, there is no risk of systemic local anesthetic toxicity and a high spinal anesthetic is less likely to be persistent or produce neurologic sequelae because the amount of drug injected is the appropriate amount for the subarachnoid space. Although there is uptake of the drug into the maternal bloodstream and transplacental passage to the fetus, the blood and tissue levels achieved are much smaller than with epidural anesthesia.[18] Many anesthetists believe that the quality of anesthesia is better with spinal anesthesia and that there is less discomfort with exteriorization of the uterus. Postoperative analgesia can be provided by injecting a small dose of morphine (0.2 to 0.5 mg) along with the local anesthetic agent.

Among the disadvantages of spinal anesthesia is the fact that this is usually a single injection procedure. Thus, if the operation lasts longer than the drug selected, heavy sedation or general anesthesia may be required for the completion as there is no opportunity to reinforce the block. If the procedure is much shorter than anticipated, the recovery time is prolonged. Although the faster onset of anesthesia is an advantage in some circumstances, the onset of hypotension may be precipitous and profound. This may compromise a fetus with marginal uteroplacental perfusion. Narcotic analgesics, for example, morphine, administered with the spinal anesthetic, pose a risk of delayed respiratory depression many hours after injection. The possibility of a post–lumbar-puncture headache is obviously greater after spinal anesthesia than after epidural anesthesia.

The precise technical details of performing spinal anesthesia for cesarean section will vary, but generally adhere to the following outline. Once the patient has arrived in the operating room appropriate monitors are applied and baseline values noted. Oxygen by face mask or nasal prongs is administered and an intravenous fluid bolus of 15 to 30 mL per kg of lactated Ringer's or other balanced salt solution is given shortly before the block. On occasion, a colloid may be preferred or used as part of the fluid load. Some anesthesiologists prefer to also give 25 to 50 mg of ephedrine intramuscularly as part of their hypotension prophylaxis routine. The patient is placed in the lateral decubitus position, or the sitting position if landmarks are not clear or if the lumbar interspaces cannot readily be opened in the lateral position, and a 25- or 22-gauge needle is placed in the subarachnoid space at the L3 to L4 or L2 to L3 interspace. The selected drug is injected and the needle removed. The parturient is then placed supine with left uterine displacement. The level is determined by the amount of drug injected and by properly positioning the patient with an understanding of the curvatures inherent in the spinal column. A table that is level or that has a slight degree of Trendelenburg position is preferred. This should achieve a level between the fourth and sixth thoracic dermatome in most patients. This is desirable even though the surgical procedure itself is low in the abdomen as traction on the peritoneum frequently causes discomfort and levels at least this high are required to reduce this.

The choice of drug will depend on the estimated duration of the cesarean section and the preference of the anesthesiologist. It is generally believed that the pregnant patient requires less drug to achieve a given spinal level than her nonpregnant counterpart. This is because the spinal subarachnoid space is probably decreased in size in pregnancy, the lumbar lordosis is accentuated, thus facilitating cephalad spread of the hyperbaric drug, and the sensitivity of nerve tissue to local anesthetics appears to be increased.[7] Among the commonly used ester-linked local anesthetics are procaine and tetracaine (Novacaine and Pontocaine). Procaine is a rapid onset drug with a duration of surgical anesthesia of 30 to 45 minutes. Tetracaine is a more potent agent with an onset of 5 to 10 minutes and a duration of 60 to 120 minutes. Some anesthesiologists combine the two drugs to gain rapid onset and longer duration. The duration of either may be prolonged by 30 to 50% by the addition of a vasoconstrictor such as epinephrine or phenylephrine. The amide local anesthetic lidocaine is quite popular and is also a rapid onset agent with a duration of approximately 40 to 75 minutes. Bupivacaine is the newest drug for spinal anesthesia in the United States and is rapidly gaining popularity as it has a rapid onset with a duration similar to tetracaine, yet post-surgical recovery from the block seems to be more rapid. All of these drugs are rendered hyperbaric by the addition of glucose. The ability of a vasoconstrictor to prolong spinal anesthesia with the amide local anesthetics is currently a matter of controversy.[19, 29]

EPIDURAL ANESTHESIA

The use of epidural anesthesia for cesarean section has increased significantly over the last two decades. This may be due to the fact that it is more widely taught than previously and many patients about to have a cesarean section already have an epidural catheter in situ that was used for labor analgesia. Epidural anesthesia may also be selected because of its specific advantages. Epidural anesthesia differs from spinal anesthesia in that a needle or catheter is placed in the epidural space and the local anesthetic finds access to the nerves by entering the dural cuffs surrounding the emerging nerve roots via arachnoid villi that penetrate the dura in this region.[27] The spread of anesthesia is therefore more volume dependent and not related to specific gravity differences between local anesthetic solution and spinal fluid. This requires approximately ten times the volume and five to ten times the dose of drug used for spinal anesthesia.

One of the principal advantages of epidural anesthesia is the ability to gradually advance and titrate the block when a catheter is in place. This coupled with its slower onset allows time for both endogenous and exogenous compensation for the sympathetic blockade, thus avoiding precipitous hypotension and reduction in uteroplacental blood flow. This ability to maintain hemodynamic stability makes continuous epidural anesthesia a leading choice for patients with severe preeclampsia. It has been demonstrated that intervillous blood flow may actually be increased in patients with this disorder.[16] Continuous epidural anesthesia allows one to reinforce a weak block and to continue the anesthetic regardless of the duration of the procedure. The degree of motor blockade is less intense for a given level and this may prove to be advantageous for multiple gestations in which a high block may impair ventilation. The muscle pump in the lower extremities may remain intact and thus reduce the incidence of phlebothrombosis. Postoperative analgesia may be instituted with a variety of epidural narcotic regimens and of course, there should be no occurrence of post–lumbar-puncture headache unless there is an unintentional dural puncture.

The slower onset of epidural anesthesia may prove to be a disadvantage in some situations, for example, a patient who is rapidly dilating with a double footling breech presentation. There is an obligatory test dose time of from 3 to 5 minutes plus that actual onset time of the surgical anesthetic dose of from 10 to 20 minutes. Much larger amounts of local anesthetic are required than with spinal anesthesia and if injected into an epidural vein could possibly result in systemic local anesthetic toxicity. If this dose should find its way into the subarachnoid space, a high or total spinal anesthetic would be the result. Maternal-fetal transfer of local anesthetic drug is greater than with spinal anesthesia, although with the usual amounts of drug administered should result in no significant neurobehavioral changes in the newborn.[1]

The monitoring and preparatory measures for epidural anesthesia are similar to those for spinal anesthesia as is the requirement for left uterine displacement. If an epidural catheter is not in situ from prior insertion for labor an epidural needle, usually a 17- to 18-gauge Tuohy needle, is inserted in the L2 to L3 or L3 to L4 interspace. The epidural space is identified by the loss of resistance to injection of saline or air through the needle or by the identification of negative pressure with a manometric indicator, balloon, or hanging fluid drop. Although some would proceed to administer the anesthetic (after a test dose) as a single injection, most anesthesiologists prefer the continuous technique and thus would insert a catheter 2 to 5 cm into the epidural space and remove the needle. The catheter is gently aspirated to detect the presence of blood or cerebrospinal fluid. After securing the catheter to the patient's back a test dose of local anesthetic is administered and the patient is observed quite carefully for the next 3 to 5 minutes (see Table 5). The test dose contains an amount of local anesthetic just adequate to produce a normal spinal anesthetic and perhaps a tracer, such as epinephrine, to indicate intravenous placement. By the end of the test period one should observe no evidence of spinal anesthesia, no increase in pulse or blood pressure, and the presence of a small band of analgesia in the low thoracic and upper lumbar dermatomes. The surgical dose is then administered. If given through the needle, 15 to 25 mL of solution (approximately 1 mL per segment of desired blockade) are then injected and the needle removed. The two major maternal concerns, profound cardiovascular collapse and neurotoxicity from massive intrathecal injection, can be minimized or avoided by fractional administration of the local anesthetic. This is more easily accomplished via continuous catheter technique although not impossible by the single injection technique. This merely means that the total dose is divided into aliquots of 5 to 10 mL and the patient observed for 3 to 5 minutes between aliquots for signs of intravascular injection or subarachnoid block.

The local anesthetics most commonly used are lidocaine (1.5 to 2.0%), 2-chloroprocaine (2 to 3%), and bupivacaine (0.5%). Combinations, either in sequence or simultaneous, are occasionally employed. Epinephrine 1:200,000 to 1:400,000 (5 to 2.5 μg per mL) may be added to reduce the rapidity of vascular absorption and prolong the duration of the block. The choice of drug is dependent on the desired speed on onset, expected duration, and maternal and fetal condition. 2-Chloroprocaine produces surgical anesthesia most rapidly, followed by lidocaine and then bupivacaine. Lidocaine that has been buffered to a pH of 7 or greater by the addition of 1 mEq of bicarbonate per 10 mL of local anesthetic has an onset time equivalent to 2-chloroprocaine, that is, approximately 5 minutes.[9] The approximate duration of 2-chloroprocaine is 40 to 60 minutes, lidocaine 60 to 90 minutes, and bupivacaine 90 to 180 minutes.

Epidural narcotics are now being administered intraoperatively both to provide postoperative pain relief and intraoperative supplementation. Preservative-free morphine sulfate in doses of 4 to 6 mg yields up to 24 hours of postoperative analgesia. Fentanyl in doses of 50 to 100 μg provides additional analgesia in 5 to 10 minutes with a duration of 2 to 4 hours. It may enhance the quality of epidural anesthesia during cesarean section.

Spinal anesthesia can therefore rapidly provide suitable conditions for cesarean section and is useful for elective procedures as well as certain urgent or emergent obstetric problems. When minimal maternal-fetal transfer of local anesthetic is essential this may be the technique of choice. Epidural anesthesia can similarly provide excellent conditions for cesarean section, particularly when the ability to titrate the block and hemodynamic stability is desired. When flexibility is desired, continuous epidural anesthesia is a decided advantage.

SEDATION DURING REGIONAL ANESTHESIA

Anxiety, sensation of pressure or tugging, or incomplete pain relief may indicate the use of adjuncts to the regional anesthetic technique. There is a general tendency to avoid depressant drugs prior to delivery of the infant. Reassurance and encouragement from the anesthetist are often adequate but there are times when pharmacologic intervention is appropriate. The inhalation of analgesic concentrations of nitrous oxide in oxygen or enflurane in oxygen may prove sufficient and should not prove depressant to the infant. Low-dose ketamine (0.25 to 0.5 mg per kg) will provide a modicum of analgesia and amnesia without compromising maternal reflexes or the neonate. Small doses of fentanyl (50 to 100 μg) may be administered intravenously if required. Alfentanil may prove useful in this situation, but has yet to be evaluated. More potent sedation in the form of narcotic analgesics, barbiturates, or larger doses of benzodiazepines are best reserved until after delivery of the infant. The recognition of a truly inadequate regional block is important and one should convert this situation to a general anesthetic rather than oversedate the mother in an attempt to maintain the status of regional anesthesia.

GENERAL ANESTHESIA

Although the major emphasis in obstetric anesthesia has been on regional anesthesia over the last several years, general anesthesia still plays a very important role in the management of the cesarean section patient. General anesthesia is indicated for patients presenting with acute fetal distress and no pre-existing anesthetic, hypovolemic patients, for example, bleeding placenta previa or abruptio placenta, patients with a coagulopathy, patients with certain cardiac lesions, patients who absolutely refuse regional anesthesia, and for patients in whom regional anesthesia could not be accomplished. There are relatively few contraindications to the use of general anesthesia, but it is best avoided in patients with a history of malignant hyperpyrexia, active asthma, or with abnormalities of the airway (Table 6).

The general anesthetic technique is oriented toward minimizing the maternal risk of aspiration and the possibility of neonatal depression. The patient is placed on the operating table with left uterine

Table 6. *Indications for General Anesthesia for Cesarean Section*

1. Acute fetal distress (for example, prolapsed umbilical cord)
2. Acute maternal hypovolemia (for example, placenta previa or abruptio)
3. Significant coagulopathy
4. Inadequate regional anesthesia
5. Maternal refusal of regional anesthesia

displacement and the appropriate monitors applied. Measures to reduce gastric contents or alkalinize them should have been instituted. Pre-oxygenation is instituted via a well-fitting mask for approximately 5 minutes. If the patient is reluctant to breathe through the mask for this period of time, she may be allowed to breathe room air until just before induction and then asked to take four vital-capacity–type breaths. This will give her the same oxygen reserve as the traditional method.[25] A small dose of a nondepolarizing muscle relaxant is given 3 to 5 minutes prior to induction to prevent fasciculations from succinylcholine. Induction is carried out after the abdomen has been prepared and draped and the obstetrician is ready. A rapid sequence induction is employed. This requires that an assistant apply pressure to the cricoid cartilage to occlude the esophagus until after an endotracheal tube has been correctly inserted and the protecting cuff has been inflated. Induction is usually achieved with 3 to 4 mg per kg of thipental or 0.5 to 1.0 mg per kg of ketamine. This dose is usually adequate to minimize maternal recall and should not negatively affect the neonate. This is immediately followed by 1.5 mg per kg of succinylcholine to achieve rapid and complete muscle relaxation and optimal intubating conditions. After intubation and verification of bilateral breath sounds, the surgery may begin. The anesthetic is maintained with nitrous oxide in a concentration of 50% or less with oxygen and a low concentration of volatile agent, for example, halothane, enflurane, or isoflurane. The volatile agent decreases maternal recall and reduces the high catecholamine levels found with light anesthesia, thus improving uterine blood flow.[28] These low concentrations are adequate as the anesthetic requirement is decreased by 20 to 30% during pregnancy and uterine tone is minimally affected. Muscle relaxation is maintained with any of the nondepolarizing agents or a succinylcholine infusion. The newer, shorter-acting drugs such as vecuronium and atracurium are quite useful for this operation. Muscle relaxants do not cross the placenta in quantities significant enough to affect the infant with the usual clinical doses. After the infant is delivered, the volatile agents are discontinued to allow for optimal uterine involution and the nitrous oxide concentration is usually increased. Narcotics and sedatives are added to ensure adequate anesthetic conditions. At the conclusion of the procedure any residual nondepolarizing neuromuscular blockade is reversed with neostigmine, endrophonium, or pyridostigmine and an anticholinergic to blunt their muscarinic side effects. Extubation is accomplished when the patient has regained her protective reflexes, can maintain her own airway, and responds to verbal command.

A variety of maternal complications may occur with general anesthesia. The most worrisome are the regurgitation and aspiration of gastric contents and failure to secure the maternal airway. Although the former has garnered the most attention in the literature, the latter is of equal, if not greater, significance. Measures to reduce the risk of aspiration have been previously discussed. The patient with an apparently difficult airway should have an awake or sedated awake intubation, perhaps guided by the use of a fiberoptic bronchoscope. Many difficult airway problems are not identified prior to induction and alternate plans need to be in place for the unexpected failured intubation. These include mask ventilation with maintained cricoid pressure, cricothyroid membrane puncture with a large bore intravenous cannula and jet ventilation with oxygen, cricothyrotomy, tracheotomy, or awakening the patient and either performing an awake intubation or converting to a regional technique when feasible.[20] Other complications include bronchospasm, hypertension and its sequelae, post-extubation laryngeal edema, and prolonged duration of muscle relaxants due to interaction with magnesium sulfate or aminoglycoside antibiotics.

The neonate should not be asleep as the result of general anesthetic induction agents, such as pentothal, if these are kept in the recommended clinical range because they are largely removed by the first pass through the fetal liver from the umbilical vein. Further dilution of the drug occurs with blood returning from the fetal extremities and the intracardiac shunts and the ductus arteriosis lead to a minimal exposure to the brain. Repeated doses or excessive doses obviously may result in some neonatal depression. The inhaled agents should not depress the healthy neonate as long as induction to delivery time is not excessive. If it exceeds 10 minutes, nitrous oxide saturation begins to occur and the infant may demonstrate drowsiness in the first few minutes of life. If adequate ventilation is not established, diffusion hypoxia may ensue. There has been a great deal of concern about nitrous oxide's effect as an inhibitor of methionine synthetase.[2] The brief period of exposure at cesarean section should not result in significant impairment although this has yet to be scientifically documented.

General anesthesia obviously has maintained great utility in obstetric anesthesia, particularly for either maternal or fetal emergency. When regional anesthesia is not desirable or possible it is the most viable alternative. Although a number of complications are potentially possible, these can be minimized by proper attention, monitoring, and observation.

LOCAL ANESTHESIA

The use of local anesthesia for cesarean section is all but a forgotten art. It is rarely demonstrated in major teaching institutions today although some authors refer to it for some unusual circumstances.[12] The advantages of being able to begin the procedure without having to await the arrival (and the hazards) of an anesthetist are certainly outweighed by the limitations of the technique. When used with a long midline abdominal incision, minimal application of retractors, and closure of the uterus in situ rather than extra-abdominally, it is possible to complete an abdominal delivery without excessive difficulty. However, the current popularity of the Pfannenstiel incision and uterine exteriorization for closure probably make this technique virtually useless. If a life-threatening emergency exists and the obstetric anesthesiologist is not immediately available, one could begin the procedure with a field block and achieve delivery of the infant, employing general anesthesia for the closure. Certainly when working in underprivileged areas this may be the only means for providing anesthesia as an anesthetist may not be available. Such individuals should refer to standard texts for the recommended technique.

The major patient complication is obviously discomfort. This can lead to straining and cause difficulty for the operator. The anesthetist asked to assist such a patient is faced with providing anesthesia without the opportunity to adequately assess the patient. The potential advantages are an immediate start and possibly the avoidance of problems associated with major regional or general anesthesia. Current statistics on the use of anesthesia for cesarean section do not refer to the use of this technique.

The available options for cesarean section anesthesia are spinal, epidural, and general anesthesia. Each method has been enhanced over the years to provide better operating conditions and increased maternal and fetal safety. The choice is made primarily by the requirements of the situation as each can be provided with nearly equivalent safety by today's obstetric anesthesiologist.

REFERENCES

1. Abboud TK, Nagappala S, Murakawa K, et al: Comparison of the effects of general and regional anesthesia for cesarean section on neonatal neurologic and adaptive capacity scores. Anesth Analg 64:996–1000, 1985
2. Baden JM, Rice SA, Serra M, et al: Thymidine and methionine syntheses in pregnant rats exposed to nitrous oxide. Anesth Analg 62:738–741, 1983
3. Bassell GM: Anesthesia for cesarean section. Clin Obstet Gynecol 28:722–734, 1985
4. Clark RB, Seifen AB: Complications of obstetrical anesthesia. Semin Anesth 1:155–167, 1982
5. Cohen SE: The aspiration syndrome. Clin Obstet Gynaecol 9:235–254, 1982
6. Cohen SE, Jasson J, Talafre ML, et al: Does metoclopramide decrease the volume of gastric contents in patients undergoing cesarean section? Anesthesiology 61:604–607, 1984
7. Datta S, Lambert DH, Gregus J, et al: Differential sensitivities of mammalian nerve fibers during pregnancy. Anesth Analg 62:1070–1072, 1983
8. Davies AO: Blood crossmatch for cesarean section. Can Anaesth Soc J 28:491–492, 1981
9. DiFazio CA, Carron H, Grosslight KR, et al: Comparison of pH-adjusted lidocaine solutions for epidural anesthesia. Anesth Analg 65:760–764, 1986
10. Endler GC, Donath RW: Inflation device to prevent aortocaval compression during pregnancy. Anesth Analg 64:1015–1016, 1985
11. Eyler SW, Cullen BF, Murphy ME, et al: Antacid aspiration in rabbits: A comparison of Mylanta and Bicitra. Anesth Analg 61:288–292, 1982
12. Friedman AJ, Haseltine FP, Berkowitz RL: Pregnancy in a patient with cystic fibrosis and idiopathic thrombocytopenic purpura. Obstet Gynecol 55:511–514, 1980
13. Gissen AJ, Datta S, Lambert D: The chloroprocaine controversy II. Is chloroprocaine neurotoxic? Reg Anaesth 9:135–145, 1984

14. Gonik B, Cotton D, Spillman T, et al: Peripartum colloid osmotic pressure changes: Effects of controlled fluid management. Am J Obstet Gynecol 151:812–815, 1985
15. Hughes SC, Ward MG, Levinson G, et al: Placental transfer of ephedrine does not affect neonatal outcome. Anesthesiology 63:217–219, 1985
16. Jouppila P, Jouppila R, Hollmen A, et al: Lumbar epidural analgesia to improve intervillous blood flow during labor in severe preeclampsia. Obstet Gynecol 59:158–161, 1982
17. Kenepp NB, Kumar S, Shelley WC, et al: Fetal and neonatal hazards of maternal hydration with 5% dextrose before caesarean section. Lancet 1:1150–1152, 1982
18. Kuhnert BR, Philipson EH, Pimental R, et al: Lidocaine disposition in mother, fetus, and neonate after spinal anesthesia. Anesth Analg 65:139–144, 1986
19. Leicht CH, Carlson SA: Prolongation of lidocaine spinal anesthesia with epinephrine and phenylephrine. Anesth Analg 65:365–369, 1986
20. Lyons G: Failed intubation. Six years' experience in a teaching maternity unit. Anaesthesia 40:759–762, 1985
21. Milsom I, Forssman L, Biber B, et al: Maternal haemodynamic changes during caesarean section: A comparison of epidural and general anaesthesia. Acta Anaesthesiol Scand 29:161–167, 1985
22. Moore TR, Key TC, Reisner LS, et al: Evaluation of the use of continuous lumbar epidural anesthesia for hypertensive pregnant women in labor. Am J Obstet Gynecol 152:404–412, 1985
23. Morishima HO, Pedersen H, Finster M, et al: Bupivacaine toxicity in pregnant and nonpregnant ewes. Anesthesiology 63:134–139, 1985
24. Myers RR, Kalichman MW, Reisner LS, et al: Neurotoxicity of local anesthetics: Altered perineural permeability, edema, and nerve fiber injury. Anesthesiology 64:29–37, 1986
25. Norris MC, Dewan DM: Preoxygenation for cesarean section: A comparison of two techniques. Anesthesiology 62:287–289, 1985
26. Reisner LS: Type and screen for cesarean section: A prudent alternative. Anesthesiology 58:476–478, 1983
27. Shantha TR, Evans JA: The relationship of epidural anesthesia to neural membranes and arachnoid villi. Anesthesiology 37:543–557, 1972
28. Shnider SM, Levinson G: Anesthesia for cesarean section. *In* Shnider SM, Levinson G (eds): Anesthesia for Obstetrics. Baltimore, Williams & Wilkins, 1979, pp 254–275
29. Spivey DL: Epinephrine does not prolong lidocaine spinal anesthesia in term parturients. Anesth Analg 64:468–470, 1985
30. Seinberg WM, Farine D: Maternal mortality in Ontario from 1970 to 1980. Obstet Gynecol 66:510–512, 1985

Address reprint requests to

Laurence S. Reisner, MD
Department of Anesthesiology
University of California
San Diego Medical Center
225 Dickinson Street
San Diego, CA 92103

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Anesthetic Care of the Patient with Preeclampsia

Robert B. Lechner, MD, PhD, [*]
and H. S. Chadwick, MD [†]

Preeclampsia occurs in approximately 7% of pregnancies and affects about 250,000 American women each year.[29] Hypertensive diseases associated with pregnancy accounted for 17% of the maternal deaths in the United States from 1974 to 1978,[38] and for 50% of the deaths in Washington State from 1977 to 1981.[5] A number of studies have indicated that the majority of maternal deaths associated with hyptertension resulted from intracranial hemorrhages.[5, 33] As anesthesiologists become increasingly involved with both the prepartum and intrapartum care of these patients, an understanding of the pathophysiology of this disease and its implications for anesthetic management becomes imperative.

DEFINITIONS, DEMOGRAPHICS, AND ASSOCIATED SYNDROMES

Table 1 presents a categorization of hypertension associated with pregnancy based on classification criteria proposed by the American College of Obstetrics and Gynecology.

The term pregnancy-induced hypertension (PIH), although often used interchangeably with preeclampsia, is a more generic term and includes gestational hypertension as well as preeclampsia and eclampsia. Preeclampsia is most likely to occur in the young nulliparous patient with poor prenatal care. Other risk factors include diabetes, chronic hypertension, multiple gestation, trophoblastic dis-

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[*] Assistant Professor, University of Virginia, Charlottesville, Virginia
[†] Associate Professor, Department of Anesthesiology, University of Washington, Seattle, Washington

Table 1. *Categorization of Hypertension Associated with Pregnancy Based on Criteria Proposed by the American College of Obstetrics and Gynecology*

- I. Preeclampsia. The occurrence of hypertension with proteinuria, generalized edema, or both occurring after 20 weeks' gestation. Preeclampsia may occur earlier than 20 weeks' gestation in the presence of trophoblastic disease
  - A. Mild preeclampsia
    - 1. Blood pressure $\geq$ 140/90 mm Hg or an increase $\geq$ 30 mm Hg in systolic pressure or $\geq$ 15 mm Hg in diastolic pressure
    - 2. Proteinuria $>$ 300 mg/L for a 24-hour period, or 1–2+ on two midstream, clean catch urine samples 6 hours apart
    - 3. Generalized edema
  - B. Severe preeclampsia. Preeclampsia plus at least one of the following findings:
    - 1. Blood pressure $\geq$ 160/110 mm Hg
    - 2. Proteinuria $>$ 5 g/24 hours of 3–4+
    - 3. Oliguria with urine output $<$ 500 mL/24 hours
    - 4. Headache, cerebral disturbances, or visual changes
    - 5. Epigastric pain
    - 6. Pulmonary edema or cyanosis
  - C. Eclampsia. Preeclampsia plus one or more seizures not attributable to any other cause
- II. Gestational hypertension. The occurrence of hypertension occurring after 20 weeks of gestation without proteinuria or generalized edema
- III. Chronic hypertension. Hypertension occurring prior to 20 weeks' gestation
  - A. Chronic hypertension with superimposed preeclampsia or eclampsia
  - B. Chronic hypertension aggravated by pregnancy

ease, advanced age, or grand multiparity.[50, 60, 70] Patients who have a history of preeclampsia have a 33% chance of its recurrence with subsequent pregnancies,[8] although the disease is usually of a milder form.

Other physical signs and symptoms associated with preeclampsia include hyperreflexia, lethargy, and decreased mental status. Laboratory findings associated with preeclampsia often include an elevated hematocrit, uric acid, and creatinine. Bleeding time may be prolonged and platelet count and fibrinogen levels decreased. In severe cases, disseminated intravascular coagulation may be present or hepatic enzyme levels may be elevated. The combination of hemolysis (H), elevated liver (EL) enzymes, and low platelet (LP) count has been referred to as the HELLP syndrome and is thought by some to be a variant of preeclampsia/eclampsia,[81] and may be associated with the development of hypoglycemia.[22]

PROPOSED ETIOLOGIES

Several etiologic theories of preeclampsia have been proposed including infection,[51] abnormal immunologic response to the placenta, and prostaglandin abnormalities. Currently, there is no adequate animal model to study the condition, and this has impeded progress

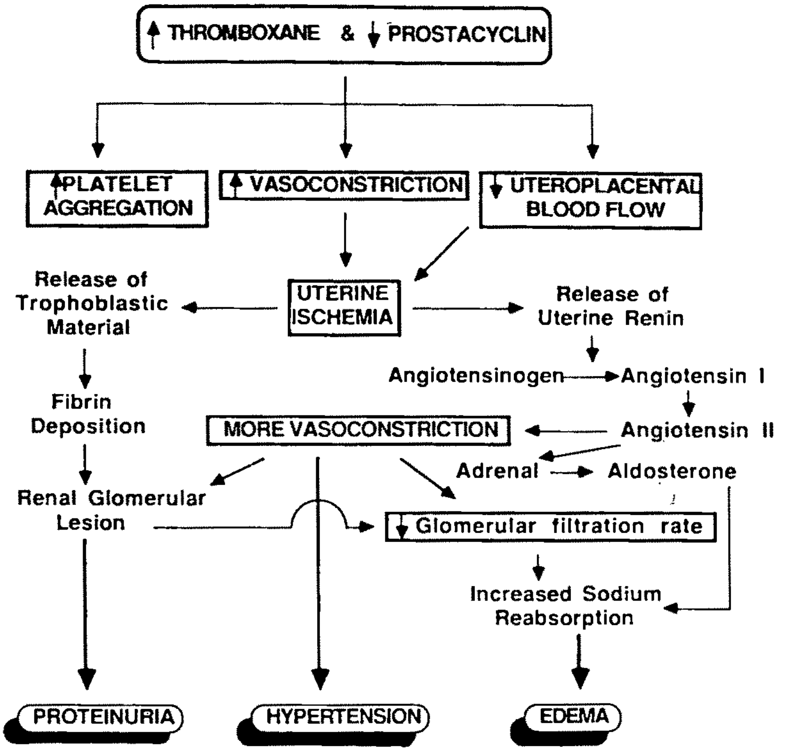

Figure 1. Contribution of the imbalance of thromboxane and prostacyclin to the clinical signs and symptoms of preeclampsia. (*From* concept of Speroff L: Toxemia of pregnancy. Mechanism and therapeutic management. Am J Cardiol 32:582, 1973. *Modified by* Gutsche BB, Cheek TG: Anesthetic considerations in preeclampsia-eclampsia. *In* Shnider SM, Levinson G (eds): Anesthesia for Obstetrics, ed 2. Baltimore, Williams & Wilkins, 1987, p 227; with permission.)

toward finding its cause(s). In most of the proposed theories, placental ischemia is postulated to play a central role in the disease process.

Abnormalities in the maternal immunologic[41,44] and vascular[42] responses to placentation have been described. These abnormalities in placental vascular development may result in placental ischemia with subsequent release of renin, activation of the angiotensin/aldosterone systems, and fluid retention and hypertension.

The role that prostaglandins play in preeclampsia has received increasing attention and has recently been reviewed.[24] Preeclampsia is associated with an underproduction of prostacyclin (a vasodilator), relative to thromboxane (a vasoconstrictor).[83] It is not clear whether these changes in prostaglandin levels are an early or late phenomenon. In a longitudinal study looking at urinary metabolites, prostacyclin metabolites were normal until the women became clinically ill, at which time the levels decreased.[83] It is possible that prostaglandins play a role in the development of clinical preeclampsia (Fig. 1), but the changes in prostaglandins may be the result of an underlying process and not a primary cause of preeclampsia.

More recently, Easterling and Benedetti[17] postulated that the early, mild hypertension that is seen in patients who later go on to develop preeclampsia is due to an elevation in cardiac output accompanied by a partial compensatory vasodilation. As the disease progresses, vasodilatory reserve is exhausted, and eventually there is a "crossover" to a high resistance state with progressively lower cardiac output, at which time the disease becomes clinically apparent. These authors have speculated that much of the renal and microvascular injury seen in the disease may be due to high-flow hemodynamic forces. Data supporting this hypothesis were recently presented,[19] but it is not yet clear what the significance of these findings are or what factors lead to the early increase in cardiac output.

PATHOPHYSIOLOGIC ALTERATIONS IN PREECLAMPSIA

Preeclampsia, almost by definition, involves some degree of renal injury. Renal blood flow and glomerular filtration rate are reduced, resulting in decreased creatinine clearance. In some patients, renal tubular enzyme excretion has been observed, indicating acute cellular injury.[27] In severe cases, cortical necrosis and acute renal failure may be present.[74]

As stated previously, edema is a characteristic of preeclampsia and appears to be due to a combination of capillary endothelial defect, increased hydrostatic pressure, and decreased plasma oncotic pressure.[3, 32, 58] There is a continuum in the degree of intravascular volume depletion seen in preclampsia. Figure 2 illustrates that central venous pressure (CVP) may remain normal in mild preeclampsia and progressively decrease as the severity of the disease increases. The decrease in intravascular volume often results in hemoconcentration and increased hematocrit.[25]

Cardiac output may be elevated in the early course of preeclampsia.[19] In the later stages, the cardiac output may fall as preload decreases; however, as seen in Figure 3, heart function may be hyperdynamic. Cardiac failure due to myocardiopathy or high afterload is rare but can be a cause of pulmonary edema, which is occasionally seen in preeclampsia.[3]

There is great variability in reported peripheral vascular resistance seen in preeclampsia ranging from low or normal to elevated.[32, 59] It is possible that this observed variability is due to the cross-sectional nature of these studies. In the early stages of the disease low resistance may be dominant but as the disease progresses, resistance may increase. Therefore, a cross-sectional study of patients may find some at an early (low or normal resistance) and some at a late (high resistance) stage in the disease process. Pulmonary vascular resistance is usually normal or low in patients with preeclampsia.[32, 59]

Coagulation disorders are common in preeclampsia. Abnormali-

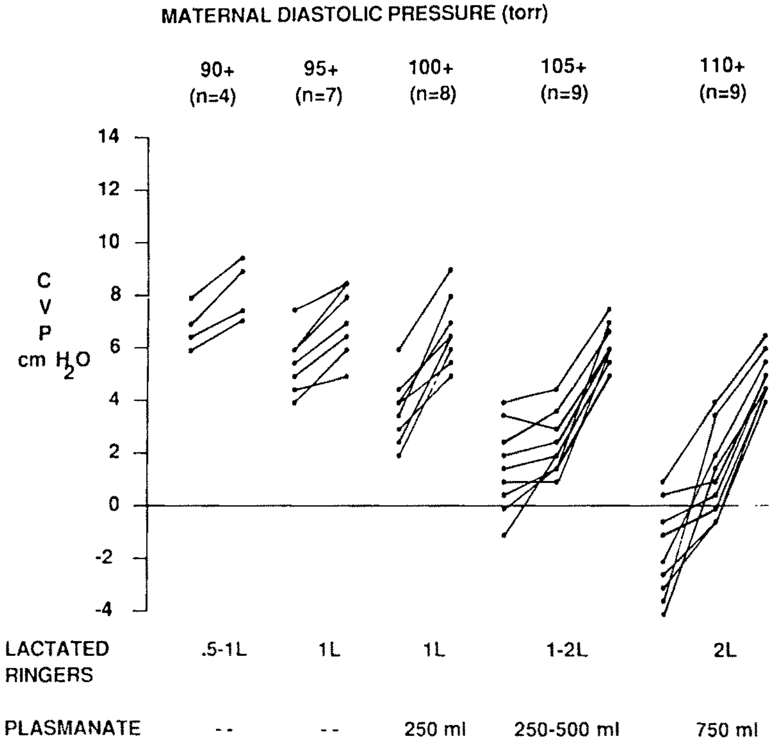

Figure 2. Central venous pressure is decreased in proportion to hypertension. The first points in each group correspond to initial measurements and the last points correspond to determinations made after fluid resuscitation and initiation of epidural block. In the last two groups, the middle points refer to the determinations made after fluid resuscitation but before epidural block. (*From* Joyce TH, Debnath KS, Baker EA: Preeclampsia—relationship of CVP and epidural analgesia. Anesthesiology 51:S297, 1979. *Modified by* Gutsche BB, Cheek TG: Anesthetic considerations in preeclampsia-eclampsia. *In* Shnider SM, Levinson G (eds): Anesthesia for Obstetrics, ed 2. Baltimore, Williams & Wilkins, 1987, p 236; with permission.)

ties include decreased platelet count, abnormal platelet function, increased platelet consumption, and prolonged thrombin time.[40, 62, 75] Preeclampsia is the most common cause of disseminated intravascular coagulation seen in the obstetric population, but fortunately its occurrence is relatively rare.[80]

Patients with severe preeclampsia may develop progressive lethargy, cortical blindness, convulsions, and coma. The etiology of these findings is unclear; however, petechial hemorrhages, multiple small cortical infarcts, and subcortical hematomas have been noted in patients who have died of the disease. The frequency with which cerebral edema complicates preeclampsia is not known, although it has been cited as an important cause of death in these patients.[4, 33] The etiology of eclamptic convulsions is also unclear but may be related

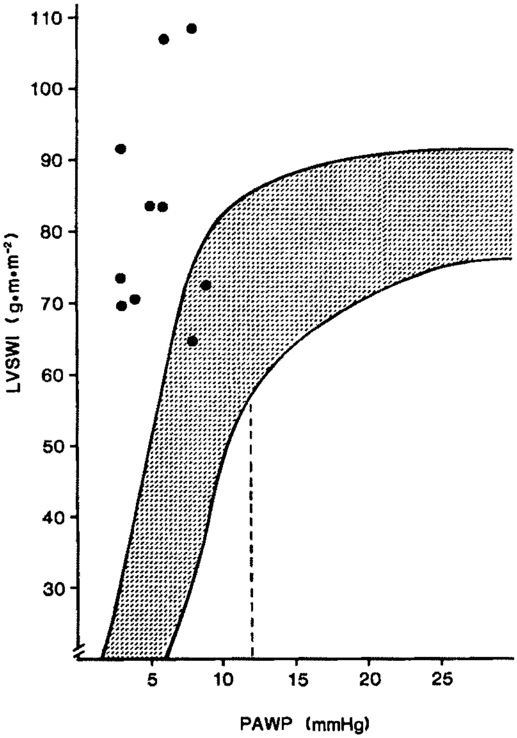

Figure 3. In severe preeclampsia, the left ventricle is often hyperdynamic and preload is low. (*From* Benedetti TJ, Cotton DB, Read JC, et al: Hemodynamic observations in severe pre-eclampsia with a flow-directed pulmonary artery catheter. Am J Obstet Gynecol 136:465, 1980; with permission.)

to areas of cerebral ischemia that develop as a consequence of vasospasm[16] or cerebral edema.[10] Because of the morbidity and mortality associated with convulsions, seizure prophylaxis is a major component of the management of the obstetric patient. The changes in EEG seen in eclamptic patients are transient and usually resolve without sequela within 6 months.[72]

MANAGEMENT OF THE OBSTETRIC PATIENT

If signs of preeclampsia develop prior to fetal lung maturity, the goal of obstetric management is to control blood pressure, maintain organ perfusion and function, provide an optimal fetal environment, and maintain the pregnancy as long as possible without compromising maternal or fetal well-being. This is usually accomplished with bed rest (preferably in the left lateral decubitus position), appropriate hydration, and antihypertensive therapy, if necessary. If maternal or fetal condition begins to deteriorate the primary objectives are to prevent seizures, control blood pressure, maintain organ perfusion (especially uterine and renal), and to deliver the fetus.

Seizure Control

The first reported use of magnesium to prevent recurrence of seizures in eclamptic patients was in 1925,[46] and has since become the mainstay of seizure prophylaxis.[63] Though benzodiazepines and chlormethiazole are used in other parts of the world, magnesium sulfate remains the drug most commonly used in the United States. Parenteral magnesium therapy is usually initiated with a bolus of 2 to 4 g over 15 minutes followed by an infusion of 1 to 3 g per hour. The normal plasma concentration of magnesium is 1.5 to 2.0 mEq per L, and the therapeutic range for seizure prophylaxis is 4 to 8 mEq per L. Higher plasma concentrations result in predictable effects and include first-degree heart block and widened QRS complexes (5 to 10 mEq per L), loss of deep tendon reflexes (10 mEq per L), respiratory insufficiency (15 mEq per L), and cardiac arrest (25 mEq per L). Magnesium intoxication can be treated with parenteral calcium administration.

Magnesium has a number of properties including smooth muscle relaxation and neuromuscular blocking effects. Neuromuscular blockade is a result of decreased acetylcholine release from the nerve terminus, decreased depolarization of the end plate from the acetylcholine that is released, and direct depression of muscle contractility.[7] Considerable controversy exists regarding the anticonvulsant and the central-nervous-system depressant effects of magnesium sulfate. Some studies indicate that magnesium has no effect on experimentally induced seizure foci[45] or on the EEG pattern of patients with preeclampsia or eclampsia.[71] Despite the paucity of evidence for central anticonvulsant properties, widely held clinical experience supports its use in prophylaxis against eclamptic convulsions. Magnesium is known to increase the production of prostacyclin,[79] and because low prostacyclin levels may contribute to the pathophysiology of preeclampsia, magnesium may have a beneficial effect by this mechanism.

Side effects of magnesium therapy include flushing, nausea and vomiting, prolongation of bleeding time, decreased fetal heart rate variability, and tocolysis.[39,49] Some reports indicate that magnesium therapy may decrease the effect of endogenous vasopressors such as angiotensin II and norepinephrine,[47] and may produce hypotension either alone[6] or in combination with antihypertensive medications[78]; however, it has not proved to be effective in treating hypertension in most preeclamptic patients.

Blood Pressure Control

Though preeclamptic patients are frequently edematous, they often have significant intravascular volume depletion. Careful rehydration is required to reverse oliguria and may by itself result in a limited lowering of arterial pressure.[67] Diuretics have been used in an attempt to maintain renal output but should only be used in the unusual circumstance of congestive heart failure or impending renal failure in a patient with adequate intravascular volume. Pharmacologic control of blood pressure is usually initiated if it remains at 170/110 or higher. The primary objective is to avoid intracranial hemorrhage.

Antihypertensive agents most commonly used in the management of PIH include α-methyl dopa and hydralazine. These agents have been popular because of their ability to maintain renal and uterine blood flow. Sodium nitroprusside, nitroglycerin, and trimethaphan are used for short-term, acute situations. Care must be exercised to not reduce blood pressure too rapidly or by more than 25% because uteroplacental blood flow may be reduced and the fetus severely compromised. As the hemodynamic variations of PIH become more apparent, agents are being used to treat specific hemodynamic abnormalities. For example, β-adrenergic antagonists (inderal or atenolol) are being used in treating high output/low resistance states, whereas the more traditional agents such as α-methyl dopa and hydralazine are being used for low output/high resistance states.[20] The mixed α- and β-adrenergic antagonist labetalol has been used with some success in the acute management of hypertension in these patients.[52] A number of other agents are being evaluated for the management of PIH and include serotonergic antagonists (ketanserin), calcium channel antagonists (nifedipine), and angiotensin-converting enzyme inhibitors (captopril), either alone or in combination.[48, 55, 77]

MONITORING AND FLUID RESUSCITATION

As our understanding of the pathophysiology of PIH increases, the need for more accurate hemodynamic data on which to base management decisions has become apparent. Given the expertise that anesthesiologists have with invasive monitoring and acute hemodynamic control, it is not surprising that obstetricians are more frequently requesting the services of anesthesiologists to assist with the care of patients with severe preeclampsia.

Invasive Arterial Pressure Monitoring

Blood pressure determinations are an integral component in the classification of preeclampsia. The classifications of preeclampsia are based on auscultative blood pressure cuff determinations; however, it is not uncommon to find automated (oscillometric) blood pressure devices being used in the obstetric suite. Many health care providers are unaware of the potential errors in determining blood pressure (especially diastolic) using oscillometric devices, therefore it is recommended that manual (auscultative) determinations be made periodically and these be used for therapeutic decisions and as the standard against which other methods can be compared.

Arterial cannulation in the patient with PIH may be helpful in a number of circumstances, including the need for repeated arterial blood gas determinations (for example, pulmonary edema) or other laboratory studies, difficulty in obtaining accurate cuff pressures (for example, obesity), beat-to-beat determinations of blood pressure (for example, use of nitroprusside), and induction of anesthesia in which rapid blood pressure changes may occur. Direct determination of arterial pressure, although the most accurate method of determining blood pressure, can yield inaccurate results.

Artifactual increases in recorded systolic, and to a lesser extent decreases in diastolic pressures, occur if there is "ringing" in the catheter/transducer system. The propensity for a system to "ring" is related to its physical properties (resonance frequency) and the hemodynamic signal, and is exacerbated if small air bubbles exist in the system or if the heart is hyperdynamic or tachycardic.[26] Error can also be introduced if the transducer is not properly calibrated and zeroed at the level of the heart.

Invasive Venous Pressure Monitoring and Fluid Resuscitation

Patients with mild symptoms of preeclampsia will rarely have significant intravascular volume deficits and consequently can usually be managed by giving fluids at maintenance rates. Epidural anesthetic techniques can be safely used in these patients with conservative intravascular volume expansion and slow initiation of the block. Invasive monitoring is rarely indicated in patients with mild preeclampsia. Patients who have developed severe disease with signs of intravascular volume depletion, as indicated by elevated hematocrit, high diastolic blood pressure (see Fig. 2), and low urine output, can present a significant challenge. Obstetric fluid management usually involves giving intravascular fluids at maintenance rates with small fluid boluses (250 to 500 mL of balanced electrolyte solution) to treat decreases in urine output. If urine output does not increase appropriately then a direct measure of central filling pressure is indicated for rational fluid management and anesthetic induction.

The decision of whether to place a central venous or pulmonary artery (PA) catheter can be a difficult one. If the patient demonstrates signs of pulmonary edema or severe oliguria (urine output < 20 mL per hour) unresponsive to small fluid challenges, a PA catheter may prove helpful, allowing determination of cardiac output and left-sided filling pressures. The correlation between CVP and pulmonary artery wedge pressure (PAWP) is known to be very poor in many preeclamptic patients.[13] If fluid resuscitation is continued using only the CVP as a guide, there is a significant risk of the patient developing pulmonary edema because, as illustrated in Figure 4, changes in CVP may not reflect changes in PAWP.[2] For this reason, if oliguria persists despite an adequate CVP (CVP > 6 mm Hg) consideration should be given to placing a PA catheter.

Considerable controversy exists regarding optimal management of the oliguric patient once a PA catheter has been placed. Kirshon et al[43] believe that colloid osmotic pressure (COP) should be the primary guide to fluid resuscitation. They advocate giving 25% albumin until the COP is greater than 17 mm Hg. Once this is achieved then PAWP

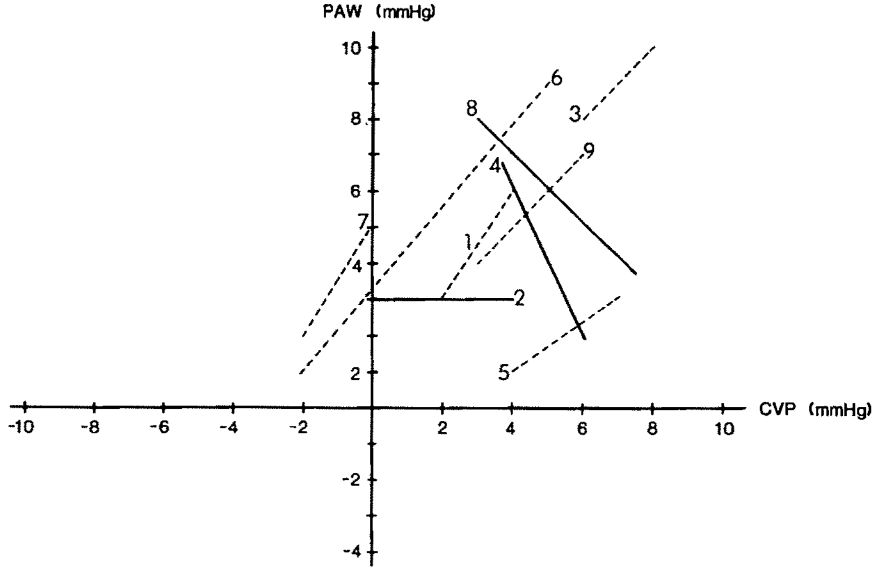

Figure 4. The relationship between CVP and PAWP in nine patients is shown. In six patients there were parallel changes in CVP and PAWP; however, in three patients there were not. (*From* Benedetti TJ, Cotton DB, Read JC, et al: Hemodynamic observations in severe pre-eclampsia with a flow-directed pulmonary artery catheter. Am J Obstet Gynecol 136:465, 1980; with permission.)

is optimized (PAWP = 10 to 15 mm Hg) and blood pressure controlled, using additional colloid solution (5% albumin), diuretics, and a vasodilator (hydralazine) as necessary.

Clark et al[11] recommend using lactated Ringer's solution as the resuscitation fluid combined with preload and afterload reduction with nitroglycerin or hydralazine. In their report, if PAWP was low (1 to 7 mm Hg) and systemic vascular resistance (SVR) mildly elevated, then only fluids were given. If PAWP was normal to elevated (9 to 18 mm Hg) and SVR normal, then fluids were given in addition to vasodilator therapy. If PAWP and SVR were elevated, then fluid restriction and afterload reduction were initiated.

With delivery of the fetus and placenta, the signs and symptoms of preeclampsia may begin to abate; however, during the next 24 to 48 hours, CVP and PAWP may rise and COP reach its nadir.[3, 64, 84] The first 24 to 48 hours following delivery is the time when pulmonary edema is most likely to occur. For this reason it is important to continue to monitor central filling pressures during the postpartum stage of the disease.

Conventional anesthetic teaching has stressed the importance of vigorous fluid resuscitation (with arbitrary CVP or PAWP endpoints) prior to initiating a neuraxial anesthetic.[66] This approach can, however, increase the risk of developing pulmonary edema, especially in the postpartum period when the anesthetic block resolves and sympathetic tone returns. Most patients with severe preeclampsia have very low central filling pressures (CVP readings of −2 to −3 mm Hg are not uncommon). Our approach in managing these patients is to administer fluids to increase filling pressure by a small amount (2 to 3 mm Hg). If significant volumes of crystalloid solution (> 1000 mL) are required to accomplish this, then the addition of colloid solutions may be desirable. If and when lumbar epidural anesthesia or analgesia is initiated, additional fluid is given, as required, in order to maintain filling pressures at preinduction levels. Using this approach we have found it possible to administer regional anesthesia safely without hypotension while giving the patient a minimal amount of fluid. Pharmacologic intervention is directed at controlling the particular hemodynamic abnormality as indicated by cardiac output, SVR, and PAWP determinations.

The risks associated with the placement of a CVP or PA catheter must be considered when deciding the need for invasive monitoring. These risks include arterial puncture with hematoma formation and possible airway compromise, neurologic injury, pneumothorax, hemothorax, and arrhythmias. A PA catheter carries additional risks of pulmonary infarction or pulmonary artery rupture. In skilled hands these complications are rare but are potentially devastating. Cannulation of the internal jugular vein can be difficult in the preeclamptic patient because of generalized edema obscuring landmarks and low intravascular volume reducing the size of the internal jugular vein.

Because of the potential problems with internal jugular cannulation, the CVP catheter is introduced through an antecubital vein if the probability of needing to place a PA catheter seems low. The right basilic vein usually allows easy passage of the catheter into a superior vena cava. Occasionally passing the catheter beyond the shoulder is difficult but can be facilitated by abducting the arm and having the patient rotate her neck toward the arm being used. If a PA catheter is necessary or will likely become necessary, then the internal jugular vein is usually used for access.

As with direct arterial pressure monitoring, errors can be introduced by catheter/transducer resonance and improper calibration and zeroing of the transducer. Because a 1 to 2 mm Hg error in CVP or PAWP measurements can have significant therapeutic implications, extreme care must be used in the interpretation of the information obtained.

Noninvasive measurements of cardiac output using impedance measurements and Doppler imaging are now possible; however, these techniques are of limited use in the anesthetic management of patients with preeclampsia. In pregnant patients, correlation of cardiac output determination using the impedance and thermodilution techniques is poor,[18] and the Doppler technique though accurate,[21] does not give PAWP measurements that are needed for optimal fluid and pharmacologic management.

ANALGESIA FOR LABOR AND VAGINAL DELIVERY

Historically, many patients with preeclampsia were not offered epidural analgesia for relief of labor and delivery pain because of concerns about intravascular volume and coagulation status. Currently, more preeclamptic patients are being offered and are benefiting from the advantages of epidural analgesia. If a patient does not wish to have regional analgesia or if there is a contraindication to epidural analgesia then nitrous oxide or morphine can provide analgesia during labor and a pudendal block can provide anesthesia for delivery.

There are many benefits of continuous epidural analgesia, especially for women with preeclampsia. These benefits include analgesia for both the first and second stages of labor, the ability to produce perineal anesthesia and relaxation if a forceps delivery or vacuum extraction becomes necessary, and the ability to readily induce surgical anesthesia if a cesarean section should become necessary.

A particular benefit of lumbar epidural analgesia is the increase in placental blood flow seen after its initiation. Intervillous blood flow is reduced in patients with preeclampsia.[37] This may, in part, be due to increased reactivity of uterine vessels. Studies have shown that in normal pregnancies[34] and in pregnancies complicated by preeclampsia,[36] lumbar epidural analgesia results in increased placental intervillous blood flow provided that blood pressure is maintained. This effect may be due to a reduction of endogenous catecholamine levels seen in patients receiving epidural analgesia.[1]

Retrospective studies have failed to find deleterious effects of epidural analgesia in preeclamptic patients.[54] The risks of epidural analgesia are well known to most anesthesiologists and include hypotension, headache, nerve trauma, infection, catheter breakage, and epidural hematoma. Unlike other risks, the risk of epidural hematoma may be increased in preeclamptic patients due to the coagulopathy that these patients may develop.

The incidence of paraplegia after epidural analgesia in the general surgical population is less than 1 in 10,000 patients.[14] The effect that coagulation defects in preeclamptic patients have on the risks associated with epidural analgesia are not known. In one retrospective study,[68] incidental thrombocytopenia (platelet count $< 150,000$ per mL) was seen in 15% of normal parturients. Sixty-one (58%) of these thrombocytopenic patients (platelet counts 50,000 to 150,000 per mL) received epidural analgesia and no adverse neurologic sequelae were detected. A study of 1000 consecutive vascular surgical patients receiving oral anticoagulation prior to epidural catheter placement, failed to detect adverse neurologic sequelae attributable to epidural catheter placement.[57] We are unaware of any patient with preeclampsia and associated coagulation disorder who suffered neurologic injury after epidural catheter placement. Therefore, we do not feel that coagulation disorders are an absolute contraindication to regional analgesia in these patients.

Because of the very low incidence of epidural hematoma the power of the previously mentioned studies to detect deleterious effects of epidural catheter placement is low. At the University of Washington, our practice is to obtain a bleeding time if the platelet count is less than 100,000 per mL or if coagulation studies are abnormal. This information is then used in making an assessment of the relative risks of lumbar epidural catheter placement compared with the benefits to be gained in that particular patient.

Lumbar Epidural Analgesia

Prior to placement of an epidural catheter, an appropriate history and physical examination are performed, the obstetric management plan is reviewed with the obstetricians, and the patient is informed of the risks and benefits of this form of analgesia. At least one 16-gauge or larger peripheral intravenous cannula is placed and blood is drawn for hematocrit, platelet count, creatinine, fibrinogen, and fibrin degradation products as well as type and screen. Oxygen is administered by face mask, an ECG monitor is attached, and an oscillometric blood pressure cuff or arterial line is placed. If necessary, a CVP or PA catheter is inserted and fluids are administered as outlined previously. Briefly, if central filling pressure is low, then crystalloid solution or 5% albumin is given to raise CVP or PCWP by 2 to 3 mm Hg. Resuscitation equipment (including suction) and drugs are checked and the epidural catheter is placed, usually in the L2 to L3 or L3 to L4 interspace. Coagulopathy may develop rapidly in these patients as the disease progresses, and for this reason we often place an epidural catheter prior to the actual need for analgesia.

Considerable controversy exists regarding the appropriate test dose solution to rule out intravascular or subarachnoid catheter placement. If blood or cerebral spinal fluid cannot be aspirated from the catheter, then 3 mL of 0.25% bupivacaine with epinephrine 1:200,000 (15 μg epinephrine) is injected immediately following a uterine contraction while the ECG and blood pressure are monitored for any changes. A significant increase in heart rate or a subjective feeling of apprehension or palpitation by the patient is considered positive for intravascular catheter placement; the catheter is withdrawn a short distance or replaced, and the aspiration and test dose are repeated. Some argue that epinephrine should not be used in the test dose because of the possible deleterious effects this may have on uterine perfusion. Alternate test solutions that have been proposed include subconvulsant doses of lidocaine or chloroprocaine, which when injected into normal male volunteers, produce tinnitus, a sensation of warmth, dizziness, or mental detachment.[28] These alternate test solutions have not been evaluated in laboring women (with or without preeclampsia) many of whom are anxious or have altered mental status and may not be able to reliably report subjective changes.

If no sign of subarachnoid block is seen 5 minutes after the test dose administration, then analgesia is initiated with 3 mL of 0.25% bupivacaine (without epinephrine) followed by an infusion of 0.125% bupivacaine or 0.0625% bupivacaine with fentanyl 2 μg per mL at 10 mL per hour. These solutions are equally effective at providing analgesia for labor,[9] and the infusion rate is adjusted as needed to maintain hypalgesia from the tenth thoracic to the second lumbar dermatome. Blood pressure is determined frequently during the first 30 minutes and every 15 minutes thereafter. Small doses of ephedrine (2.5 to 5.0 mg) may be given to treat hypotension, although this is rarely needed if ventricular filling pressure is maintained. If additional analgesia is required, a "top-up dose" of 3 to 5 mL 0.25% bupivacaine is given, the rate of infusion is increased, and blood pressure is checked frequently for the next 30 minutes. If additional perineal analgesia or relaxation is desired for delivery, then 5 to 10 mL of chloroprocaine (2 to 3%) or lidocaine (1 to 2%) is given in divided doses.

ANESTHESIA FOR CESAREAN SECTION

Regional Anesthesia

The advantages of lumbar epidural anesthesia include the ability to slowly induce the anesthetic, maintenance of maternal consciousness and airway reflex mechanisms, and minimal exposure of the fetus to anesthetic agents. After placement of an epidural catheter as described previously, a nonparticulate antacid is administered. The block is initiated with 2% lidocaine without epinephrine in 3 to 5-mL increments with at least 5-minute intervals between injections. The use of 2% lidocaine with epinephrine is advocated by some[30]; however, we believe that by avoiding these large doses of epinephrine, patients are less likely to shiver. Arterial, central venous, or PA pressures are observed and decreases in ventricular filling pressure are treated with judicious administration of intravenous fluid. If CVP or PCWP is maintained at 2 to 3 mm Hg above pre-anesthetic values, then hypotension is rarely observed. Treatment of hypotension (decrease in MAP > 15 to 20% of pre-anesthetic levels) is essential in preventing further compromise of an already stressed fetus. Small doses of ephedrine can be given if necessary. Anesthesia is induced more slowly in these patients than in nonhypertensive patients so that changes in blood pressure can be minimized.

The intraoperative management of the preeclamptic patient is very similar to that of the nonpreeclamptic patient. One significant difference is that fluid management is more difficult and more critical. Rapid changes in intravascular volume, such as with acute blood loss at the time of delivery, can have sudden and dramatic effects on blood pressure. For this reason large-bore intravenous access is a prerequisite. Because of increased vascular permeability and decreased plasma oncotic pressure, these patients are at risk for developing pulmonary edema in the postpartum period. After delivery of the fetus, 4 to 5 mg of preservative-free morphine is injected into the epidural space for postoperative pain control.[69] Because of the rapid onset of sympathectomy and propensity for severe hypotension, subarachnoid anesthesia in preeclamptic patients is not recommended.

General Anesthesia

Patients having general anesthesia for cesarean section require the same considerations regarding fluid resuscitation and monitoring outlined previously. The hypertensive response to trachael intubation is exaggerated in hypertensive patients, including those with PIH. Because of the risks of cerebral hemorrhage, it is important to anticipate the hypertensive response to intubation and take steps to avoid its occurrence. Nitroprusside or nitroglycerin are often required and can be safely titrated, provided beat-to-beat blood pressure measurement is available.

After placement of appropriate monitors and administration of a nonparticulate antacid, an additional airway assessment is made. The edema of preeclampsia can be quite severe and pharyngeal edema can be rapid in onset, making tracheal intubation difficult.[31] If difficulty in tracheal intubation is anticipated, then topical oral anesthesia should be applied and direct laryngoscopy performed. Based on the findings of laryngoscopy, awake intubation may be necessary. Nasal intubations are not recommended in these patients because of the risk of severe epistaxis.

If no airway difficulty is expected, then the patient is preoxygenated for 5 minutes. As with all obstetric patients, these patients must be considered to have a full stomach and therefore require rapid sequence induction of anesthesia. Defasciculating doses of nondepolarizing neuromuscular blockers are not administered. In the presence of magnesium they may produce profound relaxation, and magnesium, which is invariably given to these patients, prevents succinylcholine-induced fasciculations.[15] After the patient is prepped and draped and the obstetricians are prepared to make the skin incision, a rapid sequence induction with cricoid pressure is accomplished using thiopental or etomidate and succinylcholine. Ketamine should not be used to induce anesthesia because of the hypertension that may result. Tracheal intubation is confirmed by physical examination and presence of end-tidal CO_2. If tracheal intubation is unsuccessful, then management of the airway is conducted as depicted in Figure 5. As with all obstetric patients, arterial oxygen desaturation may occur very quickly owing to increased oxygen consumption and reduced functional residual capacity.

Trimethaphan,[12] nitroglycerin,[35] labetalol,[65] or sodium nitroprusside[73] has been used to control the hypertensive response to tracheal intubation in these patients. Each agent has advantages and disadvantages (Table 2). The choice of which agent(s) to use depends on the clinical status of the patient and the familiarity of the anesthesiologist with the use of each of these drugs.

Prior to delivery of the fetus, patients are maintained on a 50:50 mix of oxygen and nitrous oxide with up to 0.5 MAC of volatile anesthetic. After delivery, the anesthetic is converted to a nitrous oxide/oxygen/narcotic/relaxant technique. Use of a peripheral nerve stimulator to access muscle relaxation is essential. Magnesium, which is

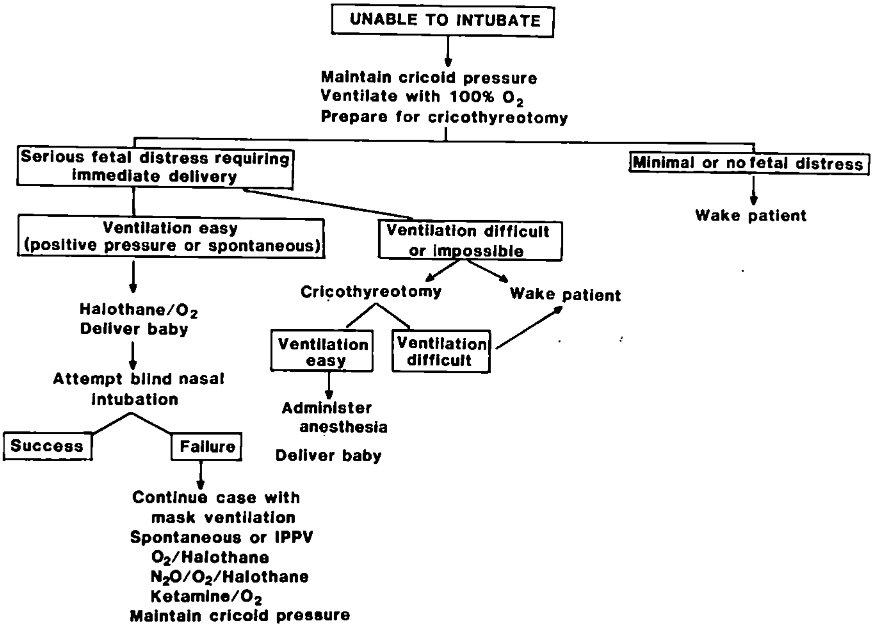
UNABLE TO INTUBATE
Maintain cricoid pressure
Ventilate with 100% O2
Prepare for cricothyreotomy
Serious fetal distress requiring immediate delivery
Minimal or no fetal distress
Wake patient
Ventilation easy (positive pressure or spontaneous)
Ventilation difficult or impossible
Halothane/O2
Deliver baby
Cricothyreotomy
Wake patient
Attempt blind nasal intubation
Ventilation easy
Ventilation difficult
Administer anesthesia
Deliver baby
Success
Failure
Continue case with mask ventilation
Spontaneous or IPPV
O2/Halothane
N2O/O2/Halothane
Ketamine/O2
Maintain cricoid pressure

Figure 5. Scheme for management of difficult intubation in the pregnant patient. (*From* Shnider S, Levinson G: Anesthesia for cesarean section. *In* Shnider SM, Levinson G (eds): Anesthesia for Obstetrics, ed 2. Baltimore, Williams & Wilkins; with permission.)

Table 2. *Properties Commonly Used of Hypotensive Agents*

DRUG & DOSE	ADVANTAGES	DISADVANTAGES
Labetalol 20 mg + 10 mg every 2 minutes up to 1 mg/kg[65]	Maintenance of uterine blood flow[52]	Nonselective α- and β-adrenergic blockage. Risk of bronchospasm and cardiac failure[53]
Nitroglycerin 0.5–10 μ/kg/ minute	No reflex tachycardia or fetal distress[35]	Increased ICP
Nitroprusside 0.2–5 μ/kg/ minute	Very rapid onset, greatest efficacy	Increased ICP and possible fetal cyanide toxicity[56]
Trimethaphan 5–50 μ/kg/ minute	Less increase in ICP than nitroprusside[76] or nitroglycerin[82]	Prolonged neuromuscular effects of succinylcholine[61]

Abbreviation: ICP, intracranial pressure.

usually given to these patients, potentiates the effect of both depolarizing and nondepolarizing neuromuscular blockers; therefore, small supplemental doses of relaxants are sufficient. Upon completion of surgery, the effects of neuromuscular blockade are reversed and the patient is extubated after she can obey commands and satisfactory muscle strength has returned. Postoperative pain can be treated using intravenous patient-controlled opioids.[23]

SUMMARY

Preeclampsia is a disease of unknown etiology and a major contributor to maternal and neonatal morbidity and mortality. In severe preeclampsia, intravascular volume depletion and susceptibility of developing pulmonary edema complicate the anesthetic management. Invasive monitors are often required for optimal patient management, with central venous or pulmonary artery pressure measurements being particularly useful for guiding volume resuscitation. In our practice, lumbar epidural blockade is the preferred method for providing analgesia and anesthesia; however, the block must be induced slowly in order to minimize sudden hemodynamic changes and to permit optimal fluid management.

REFERENCES

1. Abboud T, Artal R, Sarkis F, et al: Sympathoadrenal activity, maternal, fetal, and neonatal responses after epidural anesthesia in the preeclamptic patient. Am J Obstet Gynecol 144:915, 1982
2. Benedetti TJ, Cotton DB, Read JC, et al: Hemodynamic observations in severe preeclampsia with a flow-directed pulmonary artery catheter. Am J Obstet Gynecol 136:465, 1980
3. Benedetti TJ, Kates R, Williams V: Hemodynamic observations in severe preeclampsia complicated by pulmonary edema. Am J Obstet Gynecol 152:330, 1985
4. Benedetti TJ, Quilligan EJ: Cerebral edema in severe pregnancy-induced hypertension. Am J Obstet Gynecol 137:860, 1980
5. Benedetti TJ, Starzyk P, Frost F: Maternal deaths in Washington State. Obstet Gynecol 66:99, 1985
6 Bourgeois FJ, Thiagarajah S, Harbert GM Jr., et al: Profound hypotension complicating magnesium therapy. Am J Obstet Gynecol 154:919, 1986
7. del Castillo J, Engbaek L: The nature of the neuromuscular block produced by magnesium, J Physiol 124:370, 1954
8. Chesley LC, Annitto JE, Cosgrove RA: Prognostic significance of recurrent toxemia of pregnancy. Obstet Gynecol 23:874, 1964
9. Chestnut DH, Owen CL, Bates JN, et al: Continuous infusion epidural analgesia during labor: A randomized, double-blind comparison of 0.0625% bupivacaine/0.0002% fentanyl versus 0.125% bupivacaine. Anesthesiology 68:754, 1988
10. Clark SL, Divon MY, Phelan JP: Preeclampsia/eclampsia: Hemodynamic and neurologic correlations. Obstet Gynecol 66:337, 1985
11. Clark SL, Greenspoon JS, Aldahl D, et al: Severe preeclampsia with persistent oliguria: Management of hemodynamic subsets. Am J Obstet Gynecol 154:490, 1986
12. Connell H, Dalgleish JG, Downing JW: General anesthesia in mothers with severe pre-eclampsia/eclampsia. Br J Anaesth 59:1375, 1987

13. Cotton DB, Gonik B, Dorman K, et al: Cardiovascular alterations in severe pregnancy-induced hypertension: Relationship of central venous pressure to pulmonary capillary wedge pressure. Am J Obstet Gynecol 151:762, 1985
14. Dawkins CJM: An analysis of the complications of extradural and caudal block. Anaesthesia 24:554, 1969
15. DeVore JS, Asrani R: Magnesium sulfate prevents succinylcholine-induced fasciculations in toxemic parturients. Anesthesiology 52:76, 1980
16. Donaldson JO: Eclampsia and other causes of peripartum convulsions. *In* Neuroloygy of Pregnancy. Philadelphia, Saunders, 1978
17. Easterling TR, Benedetti TJ: Preeclampsia: A hyperdynamic disease model. Am J Obstet Gynecol 160:1447, 1989
18. Easterling TR, Benedetti TJ, Carlson KL, et al: Measurement of cardiac output in pregnancy by thermodilution and impedence techniques. Br J Obstet Gynaecol 96:67, 1989
19. Easterling TR, Benedetti TJ, Schmucker BC: Maternal cardiac output in preeclamptic pregnancies: A longitudinal study. Proceedings of the Ninth Annual Meeting of the Society of Perinatal Obstetricians, 1989, p4
20. Easterling TR, Benedetti TJ, Schmucker BC, et al: Antihypertensive therapy in pregnancy directed by noninvasive hemodynamic monitoring. Am J Perinatol 6:86, 1989
21. Easterling TR, Watts DH, Schmucker BC, et al: Measurement of cardiac output during pregnancy: Validation of Doppler technique and clinical observations in preeclampsia. Obstet Gynecol 69:845, 1987
22. Egley CC, Gutliph J, Bowes WA Jr.: Severe hypoglycemia associated with HELLP syndrome. Am J Obstet Gynecol 152:576, 1985
23. Eisenach JC, Grice SC, Dewan DM: Patient-controlled analgesia following cesarean section: A comparison with epidural and intramuscular narcotics. Anesthesiology 68:444, 1988
23. Friedman SA: Preeclampsia: A review of the role of prostaglandins. Obstet Gynecol 71:122, 1988
25. Gallery EDM, Hunyor SN, Gyory AZ: Plasma volume contraction: A significant factor in both pregnancy-associated hypertension (pre-eclampsia) and chronic hypertension in pregnancy. Q J Med 48:593, 1979
26. Gardner RM: Direct blood pressure measurement—dynamic response requirements. Anesthesiology 54:227, 1981
27. Goren MP, Sibai BM, El-Nazar A: Increased tubular enzyme excretion in preeclampsia. Am J Obstet Gynecol 157:906, 1987
28. Grice SC, Eisenach JC, Dewan DM, et al: Evaluation of 2-chloroprocaine as an effective intravenous test dose for epidural analgesia. Anesthesiology 67:A627, 1987
29. Gutsche BB, Cheek TG: Anesthetic considerations in preeclampsia-eclampsia. *In* Shnider SM, Levinson G (eds): Anesthesia for Obstetrics, ed 2. Baltimore, Williams & Wilkins, 1987, p. 225
30. Heller PJ, Goodman C: Use of local anesthetics with epinephrine for epidural anesthesia in preeclampsia. Anesthesiology 65:224, 1986
31. Heller PJ, Scheider EP, Marx GF: Pharyngolaryngeal edema as a presenting symptom in preeclampsia. Obstet Gynecol 62:523, 1983
32. Henderson DW, Vilos GA, Milne KJ, et al: The role of Swan-Ganz catheterization in severe pregnancy-induced hypertension. Am J Obstet Gynecol 148:570, 1984
33. Hibbard LT: Maternal mortality due to acute toxemia. Obstet Gynecol 42:263, 1973
34. Hollmen AI, Jouppila R, Jouppila P, et al: Effect of extradural analgesia using bupivacaine and 2--chloroprocaine on intervillous blood flow during normal labour. Br J Anaesth 54:837, 1982
35. Hood DD, Dewan DM, James FM III, et al: The use of nitroglycerine in preventing the hypertensive response to tracheal intubation in severe preeclampsia. Anesthesiology 63:329, 1985
36. Jouppila P, Jouppila R, Hollmen A, et al: Lumbar epidural analgesia to improve intervillous blood flow during labor in severe preeclampsia. Obstet Gynecol 59:158, 1982

37. Kaar K, Jouppila P, Kuikka J, et al: Intervillous blood flow in normal and complicated late pregnancy measured by means of an intravenous ^{133}Xe method. Acta Obstet Gynecol Scand 59:7, 1980
38. Kaunitz AM, Hughes JM, Grimes DA, et al: Causes of maternal mortality in the United States. Obstet Gynecol 65:605, 1985
39. Kellecher JF, Millar WL, Ellis DJ, et al: Effect of intravenous magnesium sulfate on the bleeding time. Proceedings of the 19th Annual Meeting of the Society for Obstetric Anesthesia and Perinatology, 1987, p 86
40. Kelton JG, Hunter DJS, Neame PB: A platelet function defect in preeclampsia. Obstet Gynecol 65:107, 1985
41. Khong TY, Pearce JM, Robertson WB: Acute atherosis in preeclampsia: Maternal determinants and fetal outcome in the presence of the lesion. Am J Obstet Gynecol 157:360, 1987
42. Khong TY, de Wolf F, Robertson WB, et al: Inadequate maternal vascular response to placentation in pregnancies complicated by pre-eclampsia and by small-for-gestational age infants. Br J Obstet Gynaecol 93:1049, 1986
43. Kirshon B, Moise KJ Jr., Cotton DB, et al: Role of volume expansion in severe preeclampsia. Obstet Gynecol 167:367, 1988
44. Kitzmiller JL, Benirschke K: Immunofluorescent study of placental bed vessels in pre-eclampsia of pregnancy. Am J Obstet Gynecol 115:248, 1973
45. Koontz WL, Reid KH: Effect of parenteral magnesium sulfate on penicillin-induced seizure foci in anesthetized cats. Am J Obstet Gynecol 153:96, 1985
46. Lazard EM: A preliminary report on the intravenous use of magnesium sulphate in puerperal eclampsia. Am J Obstet Gynecol 9:178, 1925
47. Lee MI, Todd HM, Bowe A: The effects of magnesium sulfate infusion on blood pressure and vascular responsiveness during pregnancy. Am J Obstet Gynecol 149:705, 1984
48. de Ligny BH, Ryckelynck JP, Mintz P, et al: Captopril therapy in preeclampsia. Nephron 46:329, 1987
49. Lin C-C, Pielet BW, Poon E, et al: Effect of magnesium sulfate on fetal heart rate variability in preeclamptic patients during labor. Am J Perinatol 5:208, 1988
50. Long PA, Oats JN: Preeclampsia in twin pregnancy—severity and pathogenesis. Aust NZ J Obstet Gynaecol 27:1, 1987
51. Lueck J, Brewer JI, Aladjem S, et al: Observation of an organism found in patients with gestational trophoblastic disease and in patients with toxemia of pregnancy. Am J Obstet Gynecol 145:15, 1983
52. Mabie WC, Gonzalez AR, Sibai BM, et al: A comparative trial of lebetalol and hydralazine in the acute management of severe hypertension complicating pregnancy. Obstet Gynecol 70:328, 1987
53. MacCarthy EP, Bloomfield SS: Labetalol: A review of its pharmacology, pharmacokinetics, clinical uses and adverse effects. Pharmacotherapy 3:193, 1983
54. Moore TR, Key TC, Reisner LS, et al: Evaluation of the use of continuous lumbar epidural anesthesia for hypertensive pregnant women in labor. Am J Obstet Gynecol 152:404, 1985
55. Naden RP, Redman CWG: Antihypertensive drugs in pregnancy. Clin Perinatol 12:521, 1985
56. Naulty J, Cefalo RC, Lewis PE: Fetal toxicity of nitroprusside in the pregnant ewe. Am J Obstet Gynecol 139:708, 1981
57. Odoom JA, Sih IL: Epidural analgesia and anticoagulant therapy. Experience with one thousand cases of continuous epidurals. Anaesthesia 38:254, 1983
58. Oian P, Maltau JM, Noddeland H, et al: Transcapillary fluid balance in pre-eclampsia. Br J Obstet Gynaecol 93:235, 1986
59. Phelan JP, Yurth DA: Severe preeclampsia I. Peripartum hemodynamic observations. Am J Obstet Gynecol 144:17, 1982
60. Porapakkham S: An epidemiologic study of eclampsia. Obstet Gynecol 54:26, 1979
61. Poulton TJ, James FM III, Lockridge O: Prolonged apnea following trimethaphan and succinylcholine. Anesthesiology 50:54, 1979
62. Pritchard JA, Cunningham FG, Mason RA: Coagulation changes in eclampsia: Their frequency and pathogenesis. Am J Obstet Gynecol 124:855, 1976

63. Pritchard JA, Pritchard SA: Standardized treatment of 154 consecutive cases of eclampsia. Am J Obstet Gynecol 123:543, 1975
64. Rafferty TD, Berkowitz RL: Hemodynamics in patients with severe toxemia during labor and delivery. Am J Obstet Gynecol 138:263, 1980
65. Ramanathan J, Sibai BM, Mabie WC, et al: The use of labetalol for attenuation of the hypertensive response to endotracheal intubation in preeclampsia. Am J Obstet Gynecol 159:650, 1988
66. Ramanathan S: Preeclampsia. *In* Obstetric Anesthesia. Philadelphia, Lea & Febiger, 1988, p 162
67. Rasmussen K, Bostofte E, Pedersen T: Volume expansion as treatment of severe pre-eclampsia. Scand J Clin Lab Invest 169 (suppl):79, 1984
68. Rolbin SH, Abbott D, Musclow E, et al: Epidural anesthesia in pregnant patients with low platelet counts. Obstet Gynecol 71:918, 1988
69. Rosen MA, Hughes SC, Shnider SM, et al: Epidural morphine for the relief of postoperative pain after cesarean delivery. Anesth Analg 62:666, 1983
70. Scott JS: Pregnancy toxaemia associated with hydrops foetalis, hydatidiform mole and hydramnios. J Obstet Gynaecol Br Emp 65:689, 1958
71. Sibai BM, Spinnato JA, Watson DL, et al: Effect of magnesium sulfate on electroencephalographic findings in preeclampsia-eclampsia. Obstet Gynecol 64:261, 1984
72. Sibai BM, Spinnato JA, Watson DL, et al: Eclampsia IV. Neurological findings and future outcome. Am J Obstet Gynecol 152:184, 1985
73. Stempel JE, O'Grady JP, Morton MJ, et al: Use of sodium nitroprusside in complications of gestational hypertension. Obstet Gynecol 60:533, 1982
74. Stratta P, Canavese C, Colla L, et al: Acute renal failure in preeclampsia-eclampsia. Gynecol Obstet Invest 24:225, 1987
75. Stubbs TM, Lazarchick J, Van Dorsten JP, et al: Evidence of accelerated platelet production and consumption in nonthrombocytopenic preeclampsia. Am J Obstet Gynecol 155:263, 1986
76. Turner JM, Powell D, Gibson RM, et al: Intracranial pressure changes in neurosurgical patients during hypotension induced with sodium nitroprusside or trimetaphan. Br J Anaesth 49:419, 1977
77. Voto LS, Zin C, Neira J, et al: Ketanserin versus α-methyldopa in the treatment of hypertension during pregnancy: A preliminary report. J Cardiovasc Pharmacol 10(suppl 3):S101, 1987
78. Waisman GD, Mayorga LM, Camera MI, et al: Magnesium plus nifedipine: Potentiation of hypotensive effect in preeclampsia? Am J Obstet Gynecol 159:308, 1988
79. Watson KV, Moldow CF, Ogburn PL, et al: Magnesium sulfate: Rationale for its use in preeclampsia. Proc Natl Acad Sci USA 83:1075, 1986
80. Weiner CP: The obstetric patient and disseminated intravascular coagulation. Clin Perinatol 13:705, 1986
81. Weinstein L: Syndrome of hemolysis, elevated liver enzymes, and low platelet count: A severe consequence of hypertension in pregnancy. Am J Obstet Gynecol 142:159, 1982
82. Writer WDR, James FM III, Stullken EH Jr, et al: Intracranial effects of nitroglycerine—an obstetrical hazard? Anesthesiology 53:S309, 1980
83. Ylikorkala O, Pekonen F, Viinikka L: Renal prostacyclin and thromboxane in normotensive and preeclamptic pregnant women and their infants. J Clin Endocrinol Metab 63:1307, 1986
84. Zinaman M, Rubin J, Lindheimer MD: Serial plasma oncotic pressure levels and echoencephalography during and after delivery in severe pre-eclampsia. Lancet 1:1245, 1985

Address reprint requests to

Robert B. Lechner, MD, PhD
Department of Anesthesiology
Health Sciences Center, Box 238
University of Virginia
Charlottesville, VA 22908

0889–8537/90 $0.00 + .20

Anesthesia for Complicated Vaginal Deliveries

*Kenneth L. Pollack, MD,**
and David H. Chestnut, MD†

Although most vaginal deliveries are uncomplicated, approximately 5% are complicated by abnormal presentation, multiple gestation, shoulder dystocia, or retained placenta. An understanding of these complicated obstetric problems allows the anesthesiologist to provide optimal care in these challenging circumstances.

ABNORMAL PRESENTATION

The breech presentation is the most common abnormal presentation, with an incidence of 1.9 to 4.2% of all deliveries.[6,8,38,46] The breech may present in one of three ways: the *frank breech* in which both hips are flexed and both knees extended; the *complete breech* in which both hips are flexed and both knees flexed; and the *incomplete breech* in which one or both hips are extended. Approximately two-thirds of breech presentations are frank breech, whereas the remaining third are evenly divided between complete and incomplete breech. The fetus in a frank breech presentation tends to remain in that presentation. The fetus in a complete breech presentation may change to incomplete breech at any time before or during labor.

Prior to 35 weeks' gestation the fetus frequently changes presentation. Beyond 35 weeks' gestation the presentation tends not to change spontaneously as a result of increased fetal size relative to amniotic fluid volume.

Prematurity is the most common problem associated with the breech presentation. At 30 weeks' gestation 13% of infants are in the

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* Fellow in Obstetric Anesthesia, University of Iowa Hospitals and Clinics, Iowa City, Iowa
† Associate Professor of Anesthesia, Obstetrics and Gynecology, University of Iowa College of Medicine, Iowa City, Iowa

breech presentation.[2] Other factors that predispose to the breech presentation are uterine abnormalities, low placental implantation, multiple gestation, and congenital anomalies (particularly hydrocephalus and anencephaly).[8]

The incidences of placental abruption and fetal distress are markedly higher with breech as compared with vertex presentation.[8] Also, there is a high incidence of *umbilical cord prolapse*. In a series of over 86,000 deliveries, Rovinsky et al[46] found an incidence of umbilical cord prolapse of 0.5% for vertex, 1.7% for frank breech, and 10.9% for complete breech presentation.

Obstetric Management

The mode of delivery of the breech infant remains controversial. Obstetricians long have recognized that breech infants suffer greater perinatal morbidity and mortality than vertex infants. In a retrospective study of 538 consecutive breech deliveries, the group of breech infants delivered by cesarean section was identified as having less morbidity and mortality than those delivered vaginally.[38] Thus it was recommended that there be more liberal use of cesarean section in the delivery of breech infants.[38,46] Early studies of neonatal outcome often failed to properly correct for the method of vaginal delivery employed (that is, total breech extraction, assisted or spontaneous delivery) and other factors associated with increased perinatal morbidity and mortality.[40] For example, the method of delivery of the aftercoming fetal head may affect neonatal outcome. One study noted that the use of Piper forceps at vaginal delivery was associated with reduced perinatal mortality of breech infants weighing between 1000 and 3000 g.[37]

At least three recent prospective, randomized studies have assessed the relative safety of vaginal delivery versus cesarean section of the breech infant.[11,12,23] These studies found a slight increase in minor birth trauma (mostly brachial plexus injuries) but no difference in Apgar scores or mortality between the vaginal delivery and cesarean section groups. It is noteworthy that these studies documented surprisingly high maternal morbidity following cesarean section. In the cesarean section groups, 36 to 49% of women suffered significant morbidity (for example, hemorrhage, infection, deep venous thrombosis). In the vaginal delivery groups maternal morbidity was less than 10%.[11,12] In a recent review of selected studies of breech deliveries, Myers and Gleicher[40] concluded that when all factors for excess neonatal morbidity and mortality are considered, there is no reduction in neonatal morbidity with routine cesarean section. These data, which suggest the relative safety of selected vaginal breech delivery, may result in a future increase in vaginal breech deliveries.

Before the obstetrician opts for vaginal delivery of an infant in the breech presentation, an attempt may be made to perform an external cephalic version. In this procedure an intravenous catheter is placed and a beta-sympathomimetic drug (for example, ritodrine or terbutaline) is administered to relax the uterus. The obstetrician then attempts to turn the fetus to a vertex presentation. The success rate for this procedure is 60 to 73%.[21,49] Although this is a relatively safe procedure, there is the potential for fetal distress secondary to an umbilical cord accident. If fetal distress occurs, the obstetrician may elect to perform an emergency cesarean section. The anesthesiologist must then anesthetize a patient with tachycardia and vasodilation secondary to a beta-sympathomimetic drug.

Should the obstetrician allow the patient with a frank breech presentation to labor, cervical dilation should be adequate to allow atraumatic delivery of the fetal head. (The dilating wedge formed by the buttocks and thighs has roughly the same diameter as the head, and results in effective dilation of the cervix.) However, in the non-frank breech presentation, the lower extremities and trunk may be delivered before there is sufficient cervical dilation to allow passage of the fetal head. The infant at greatest risk for head entrapment is the preterm infant in the non-frank breech presentation. The ratio of head circumference to abdominal circumference is greater than one prior to 32 weeks' gestation, but by 34 weeks' gestation this ratio reverses.

Total breech extraction is associated with increased neonatal morbidity and mortality.[46] But if spontaneous delivery to the level of the umbilicus is allowed, the incidence of cervical head entrapment will be minimized.[2] Therefore, assisted breech delivery is preferred over total breech extraction. Specifically, the obstetrician seeks to maintain flexion of the fetal head. Some obstetricians ask an assistant to apply transabdominal pressure on the fetal head to maintain flexion of the cervical spine during descent. Also, the Mauriceau-Smellie-Veit maneuver or the application of Piper forceps will help maintain fetal head flexion and thus decrease the likelihood of fetal head and neck trauma at delivery.[2,37]

During vaginal breech delivery, the head may become entrapped by either the cervix or the perineum. When cervical head entrapment occurs the obstetrician may request general anesthesia with a potent halogenated agent to effect cervical relaxation. Under dire circumstances, the obstetrician may perform cervical incisions (Dührssen's incisions). Rarely, the infant cannot be delivered and is returned to the uterine cavity, and emergency cesarean section is performed.

Typically, the obstetrician will perform a generous episiotomy as prophylaxis against perineal obstruction. If entrapment results from perineal obstruction, skeletal muscle relaxation may facilitate delivery.

Anesthetic Management of Vaginal Breech Deliveries

In many centers epidural analgesia is the analgesic technique of choice for labor and vaginal delivery of the breech infant. Epidural anesthesia may prolong the second stage of labor during breech delivery,[7,14,17] but it does not increase the likelihood of operative intervention. Brenner et al[8] found no difference in neonatal acid-base status and Apgar scores between those mothers who received local infiltration or pudendal block and those who received either lumbar epidural or caudal anesthesia. Crawford[17] reported an improvement in "Apgar-minus-colour" score in those infants whose mothers received lumbar epidural anesthesia versus those whose mothers received local infiltration. Others have shown no difference in neonatal outcome between epidural and local infiltration anesthesia.[7,14] These retrospective studies support the safety of lumbar epidural anesthesia during labor and delivery of the breech infant.

For the frank breech presentation, the considerations for epidural anesthesia are much the same as those for the vertex presentation. For the non-frank breech presentation, especially with a preterm fetus, a primary goal is to prevent premature maternal pushing. If the mother begins pushing before complete cervical dilation, the fetal legs and trunk may pass through a partially dilated cervix, and the head may become entrapped. To minimize the premature urge to push, the anesthesiologist should ensure sacral analgesia during the first stage of labor. Of course, while successful sacral block may prevent premature pushing, it may be accompanied by a significant motor block of the rectus abdominal muscles. This may be troublesome, since the obstetrician typically desires a spontaneous delivery to the level of the umbilicus.

On occasion it may be difficult to achieve satisfactory sacral block with a single lumbar epidural catheter. An alternative is the double catheter technique. With this method one catheter is placed in a high lumbar interspace and a second catheter is placed through the caudal canal. A small volume of dilute local anesthetic (for example, 6 mL of 0.125% bupivacaine) is injected through the lumbar catheter for relief of first stage pain. As soon as the mother has the urge to push, a slightly larger volume of a more concentrated local anesthetic solution (for example, 10 mL of 1.5% lidocaine or 2% 2-chloroprocaine) is injected via the caudal catheter. This will prevent the premature urge to push and provide superb analgesia and perineal relaxation for the second stage of labor and episiotomy. The maintenance of rectus muscle tone should allow effective maternal pushing during the second stage of labor. Low spinal anesthesia (saddleblock) or a pudendal block are reasonable alternatives for providing delivery anesthesia with or without the presence of a previously inserted epidural catheter. Low spinal anesthesia may be achieved with 3 to 4 mg of tetracaine, 15 to 30 mg of lidocaine, or 4 to 6 mg of bupivacaine.

If fetal head entrapment occurs, the obstetrician may request general anesthesia for cervical and perineal relaxation. For this reason, an anesthesiologist who is prepared to give general anesthesia should be present for every patient undergoing a vaginal breech delivery. When the patient enters the delivery room, she should be given a nonparticulate antacid (for example, 30 mL of 0.3 mol per L sodium citrate). All routine monitors should be placed. The mother should inspire supplemental oxygen during the second stage of labor. This may obviate the need for additional preoxygenation before the induction of general anesthesia. Alternatively, preoxygenation can be accomplished with four vital-capacity breaths of 100% oxygen.[41] Induction of general anesthesia can be accomplished with either 4 mg per kg sodium thiopental or 1 mg per kg ketamine, followed by 1.0 to 1.5 mg per kg succinylcholine. Cricoid pressure should be maintained until the trachea is intubated with a cuffed endotracheal tube and proper placement of the endotracheal tube is confirmed. (When head entrapment results from perineal obstruction, delivery may soon follow the administration of succinylcholine.) After intubation a high concentration (for example, ≥ 2 MAC) of a potent halogenated agent should be administered. This will result in uterine and cervical relaxation in approximately 3 minutes. (Isoflurane, enflurane, and halothane are equipotent uterine relaxants when administered in equal anesthetic doses.[39] But smooth muscle constitutes only 10 to 15% of total cervical tissue in most women.[18] Therefore, one can achieve profound uterine relaxation but limited cervical relaxation with these smooth muscle relaxants.) After delivery, it is important that uterine tone be restored rapidly to minimize blood loss. One should discontinue the potent halogenated agent immediately after delivery and begin an oxytocin infusion intravenously. (Oxytocin should not be given as a bolus, as it may cause hypotension.[30]) Finally, the patient should not be awakened until the placenta is delivered, the episiotomy is repaired, and hemostasis is secured.

Some practitioners recommend the use of direct smooth muscle relaxants (for example, amyl nitrite, magnesium sulfate, nitroglycerine) rather than general anesthesia to relieve cervical head entrapment. At this time there are no controlled studies supporting the efficacy of these drugs during delivery. In addition, amyl nitrite in oxygen is an explosive mixture.

Preparations should be made for the aggressive resuscitation of the breech infant following delivery. Breech infants tend to be more depressed than vertex infants.[8] Ideally, a separate resuscitation team headed by either a pediatrician or an anesthesiologist should be immediately available. The American Society of Anesthesiologists recently stated: "Qualified personnel, other than the anesthesiologist attending the mother, should be immediately available to assume responsibility for the resuscitation of the depressed newborn."[3] Rarely, it may be necessary for the obstetrician or the anesthesiologist attending the mother to momentarily assist in the initial care of the neonate.

If cesarean section is necessary, either regional or general anesthesia is acceptable. In situations of fetal distress, one may be able to extend previously established epidural analgesia for cesarean section. Some centers use spinal anesthesia successfully in situations of fetal distress. However, in most cases of dire distress, rapid sequence induction of general anesthesia is considered most appropriate. In the case of cesarean section of the preterm infant, uterine relaxation may be necessary to allow an atraumatic delivery via a vertical uterine incision. Similarly, uterine relaxation may be necessary in cases of certain fetal malformations (for example, hydrocephalus, sacral teratoma). Since regional anesthesia does not relax the uterus, one may favor general anesthesia in these settings.

MULTIPLE GESTATION

Multiple gestation complicates approximately 1.2% of all pregnancies. Most cases of multiple gestation are twin gestations.[29] Most pregnancies of gestation greater than two result from ovulation induction or in vitro fertilization. Of all twin gestations, approximately a third are monozygotic, and two-thirds are dizygotic. Of monozygotic twins, 1 in 25 are monoamnionotic. Monozygotic twins are at a greater risk for morbidity and mortality than dizygotic twins. Much of the increased morbidity is the result of vascular anastomoses, which may result in polycythemia and congestive heart failure in one fetus and hypovolemia in the other. In addition, monoamnionotic twins have the potential for tangling of the umbilical cords; this may compromise blood flow to one or both fetuses.

The physiologic changes of pregnancy are exaggerated with multiple gestation. Plasma volume increases 67% with twin pregnancies versus 48% with a single fetus. Total blood volume increases by 49% with twin gestation compared with 42% with single gestation.[45] The greater size of the uterus increases the severity of aortocaval compression.[20,32] Impaired venous return leads to greater lower-extremity and sacral edema.[1] There is also greater impairment of diaphragmatic excursion.[5] In extreme cases this may lead to progressive respiratory failure.

Multiple gestation pregnancies are associated with a higher rate of both antepartum and postpartum complications than are single gestation pregnancies. The incidence of preeclampsia is increased in twin gestation.[42] This is most likely a result of the increased placental mass and perhaps relative placental hypoperfusion. There is also an increased likelihood of preterm labor and delivery.[42] It is hypothesized that preterm labor results from overdistension of the uterus. Also, there is a higher incidence of uterine atony following delivery.[42] Therefore, the blood loss with a twin delivery is greater than that which occurs with delivery of a single fetus. Finally, neonatal morbidity and mortality are significantly greater for twins than singletons.[35] Much of this results from the increased rate of preterm delivery. Also, the second twin tends to be more depressed than the first owing to decreased uteroplacental pertusion or partial abruption during the delivery process and therefore has a greater need for resuscitation.

The variety of twin presentations is illustrated in Table 1. Twin presentation influences the mode of delivery. Vaginal delivery is preferred in most cases of vertex-vertex presentation.[9] If the pairing is vertex-nonvertex and the estimated fetal weight is greater than 1500 g, then twin B fares as well with vaginal as with abdominal delivery.[43] Regardless of the presentation of twin B, it may be necessary to perform internal podalic version and total breech extraction. If breech

Table 1. *Variety of Twin Presentations*

PRESENTATION	PERCENT
Vertex-vertex	41
Vertex-breech	25
Vertex-transverse	10
Breech-vertex	7
Breech-breech	6
Breech-transverse	4
Other	7

Data compiled from references 9 and 43.

extraction of twin B is performed soon after delivery of twin A, it should not place twin B at a greater risk of head entrapment and birth trauma than if spontaneous delivery is allowed, because twin A has both tested and "prepared" the passage for twin B. Often, satisfactory analgesia and pelvic and abdominal muscle relaxation (all provided by regional anesthesia) will be sufficient for version and extraction of twin B. In some situations, however, uterine relaxation is required.

If twin A has a nonvertex presentation, it is likely that a cesarean section will be performed. With the breech-vertex presentation, there is a 1% chance of locking of the fetal heads during attempted vaginal delivery. This complication has a 50% mortality rate.[13]

Anesthetic Considerations for Multiple Gestation

In 1958 Little and Friedman[35] reviewed the published literature and concluded that major conduction anesthesia for vaginal twin delivery was associated with poor neonatal outcome, as compared with either local infiltration/pudendal block or inhalation analgesia. The safety of epidural and caudal analgesia was re-evaluated two decades later. Studies by Crawford[16] and James et al[31] found no difference in neonatal acid-base status and Apgar scores between infants whose mothers received epidural analgesia versus local infiltration or pudendal block. It is now widely accepted that lumbar epidural anesthesia is safe and desirable for the vaginal delivery of twins.

If epidural analgesia is employed for vaginal delivery of twins, several factors must be considered to maximize its safety. Because of the increased uterine mass, there is greater severity of aortocaval compression.[20,32] It is therefore particularly important to maintain left uterine displacement; this will improve venous return and help maintain cardiac output and uteroplacental perfusion. Adequate prehydration of the mother is mandatory prior to epidural injection of local anesthetic. A bolus of lactated Ringer's solution (that is, ≥ 10 mL per kg for labor analgesia; ≥ 20 mL per kg for cesarean section anesthesia) should be administered before injection of the test dose. After the test dose is judged to be negative, the block should be established slowly. This will minimize hypotension. Finally, it is helpful to electronically monitor the heart rate of both fetuses before, during, and after induction of epidural anesthesia. If the membranes are ruptured, an ECG lead may be placed on the scalp of twin A, while twin B is monitored externally.

During vaginal twin delivery the considerations for epidural analgesia are similar to those for a single delivery. If a spontaneous delivery is planned (as with a vertex-vertex pairing), one may attempt to provide analgesia with minimal motor block so that the mother is able to push effectively. However, if it is likely that twin B will be delivered by internal podalic version and breech extraction, both the obstetrician and the patient will benefit from a dense sacral block. In that circumstance one may inject 10 to 15 mL of local anesthetic at the time of delivery of twin A. If epidural analgesia was not used during the first stage of labor, then low spinal anesthesia may be used.

Because uterine and cervical relaxation is occasionally required for vaginal delivery of the second twin, an anesthetist who is prepared to immediately induce general anesthesia should be present. Following delivery of twin A, if the presentation of twin B is found to be nonvertex, and the uterus is tight or the cervix has begun to contract, administration of a potent halogenated agent will relax the uterus and facilitate internal podalic version and extraction. As with the breech delivery, the mother should receive an oral antacid, have all routine monitors applied, and inspire supplemental oxygen during the second stage of labor. If general anesthesia is necessary, proceed with the application of cricoid pressure and rapid sequence induction with endotracheal intubation. After intubation, greater than or equal to 2 MAC of a potent halogenated agent should be administered. This will result in uterine relaxation within approximately 3 minutes. Following delivery, the potent agent should be discontinued to allow the uterus to contract. The patient should remain anesthetized and intubated until the placenta is delivered, the episiotomy is repaired, and hemostasis is secured.

If cesarean section is planned, either regional or general anesthesia is acceptable. If regional anesthesia is chosen, epidural is preferable to spinal anesthesia as it allows a slower onset of the sympathetic block and thus decreases the likelihood of hypotension. Any fall in blood pressure during onset of the block should be aggressively treated with increased left uterine displacement, intravenous fluid boluses, and intravenous ephedrine. If general anesthesia is chosen, one should perform preoxygenation, cricoid pressure, rapid sequence induction, and endotracheal intubation. Anesthesia is then maintained with 30 to 50% nitrous oxide in oxygen and approximately 0.6 MAC of a potent halogenated agent. The effect of a low concentration of potent agent on perioperative blood loss is controversial.[22,51] If a small concentration of potent agent increases blood loss at cesarean section, the effect is small. It is important to administer a small concentration of a potent inhalation agent to provide effective maternal amnesia.[52] Furthermore, administration of a potent halogenated agent allows the anesthesiologist to give an increased inspired oxygen concentration to the mother. This results in increased oxygen delivery to the fetus and minimizes neonatal depression.[36] Following delivery, it is possible to increase the concentration of nitrous oxide up to 70% and reduce or eliminate the concentration of the potent agent.

Gestations of more than two fetuses carry an even greater risk to both mother and infants. The cardiovascular changes of pregnancy are further exaggerated. Abdominal distension and diaphragmatic elevation can cause respiratory failure, which may be an indication for early delivery. Essentially, all viable fetuses of triplet or greater gestation are delivered abdominally in some centers. If the maternal respiratory status is marginal prior to cesarean section, general anesthesia is preferred because of the potential for further maternal respiratory embarrassment with high regional anesthesia.

SHOULDER DYSTOCIA

The diagnosis of shoulder dystocia is made after delivery of the head when impaction of the anterior shoulder against the maternal symphysis pubis occurs, preventing delivery.[48] The incidence of shoulder dystocia is 0.2 to 1.7% of deliveries of infants weighing greater than 2500 g.[4,50] Risk factors for development of shoulder dystocia include fetal macrosomia, previous infant weighing greater than 4000 g, multiparity, obesity, diabetes, post-term labor, prolonged second stage of labor, and mid-forceps delivery.[4,28]

Shoulder dystocia results in significant neonatal morbidity or mortality in up to 48% of the cases.[4,26] Morbidity is most often due to fetal hypoxia, orthopedic injury (for example, fracture of the humerus or clavicle), and peripheral nerve injury (Erb's palsy).[4] In addition to a high rate of fetal morbidity, there is increased maternal morbidity (for example, vaginal trauma, increased blood loss). Identification of risk factors alerts the obstetrician to the possibility of a shoulder dystocia. If the risk of dystocia is considered to be great (for example, estimated fetal weight greater than 4500 g) then the obstetrician may perform an elective cesarean section. If a vaginal delivery is attempted in the presence of risk factors for shoulder dystocia, then the anesthetist should be notified in order to be prepared to handle the maternal and neonatal complications that may arise. However, we emphasize that most cases of shoulder dystocia are unexpected.

Obstetric Management of Shoulder Dystocia

Upon the diagnosis of shoulder dystocia, the obstetrician will perform a series of maneuvers to facilitate delivery of the fetal shoulders. First, an assistant applies suprapubic pressure while the obstetrician applies gentle inferior and posterior pressure to the fetal head. This may allow the posterior shoulder to fall into the sacral concavity, thus making room for delivery of the anterior shoulder. If this is unsuccessful, the obstetrician may attempt to deliver the posterior shoulder over the perineum. Otherwise, the posterior shoulder is rotated 180 degrees anteriorly until it delivers (that is, the corkscrew maneuver).

If this fails, the posterior arm may be swept away and delivered. Delivery may then occur spontaneously or require rotation of the fetal trunk. If these efforts fail, a fetal clavicle may be fractured. This decreases the width of the fetal shoulders and allows spontaneous delivery.[48] An alternative to clavicle fracture, rarely used in this country, is symphysiotomy. This procedure requires local infiltration anesthesia and results in a 1.5 to 2.5-cm pelvic enlargement.[47] This may help avoid the morbidity associated with neonatal orthopedic injury. Although the latter two procedures may be helpful, they are best avoided due to the potential for serious morbidity. In contrast, a helpful noninvasive manuever unknown to some obstetricians is the McRobert's maneuver.[26] This maneuver, which is employed at the first evidence of shoulder dystocia at our hospital, places the mother in complete thigh flexion (knee-chest position). This rotates the symphysis superiorly and often alleviates the anterior shoulder impaction.

Occasionally, all maneuvers will fail to allow vaginal delivery of the infant. In such case the Zavanelli maneuver may be employed.[47] With this maneuver, the fetal head is returned to the uterus and held in place by an assistant while the obstetrician proceeds with a cesarean section. This procedure may be lifesaving for the infant and should not increase maternal morbidity beyond that for any other emergency cesarean section.[47]

Following delivery, the infant with a shoulder dystocia is likely to be severely depressed. Personnel for resuscitation of the neonate should be summoned as soon as the diagnosis of shoulder dystocia is made. The anesthetic requirements for delivering an infant at risk for shoulder dystocia are similar to a routine vaginal delivery. However, good pelvic and perineal anesthesia are essential for many of the previously mentioned maneuvers to be accomplished without excessive maternal discomfort. This can be provided with epidural or low spinal anesthesia. Pudendal anesthesia is occasionally preferred by some obstetricians as this ensures that the parturient can generate maximum pushing efforts.

On occasion, general anesthesia may be required if adequate pelvic anesthesia is lacking. Skeletal muscle relaxation of the pelvic floor by succinylcholine may facilitate delivery of the shoulders. In this circumstance one should proceed with preoxygenation (four vital-capacity breaths of 100% oxygen),[41] cricoid pressure, rapid sequence induction, and intubation with a cuffed endotracheal tube. As opposed to anesthesia for breech or twin delivery, uterine muscle relaxation is not required in this circumstance. After delivery the mother should remain anesthetized and intubated until the placenta is delivered and the episiotomy is fully repaired. Again, it should be emphasized that the anesthetist should be present at the start of the delivery because time is of the essence once the head is delivered and the shoulder becomes entrapped.

Other Abnormal Presentations

In addition to the breech presentation, one may encounter several other abnormal presentations. In the case of a *face* presentation, vaginal delivery is possible provided the mentum is anterior, but there is an increased likelihood of cephalopelvic disproportion. Most other abnormal presentations (brow, shoulder transverse) are not compatible with vaginal delivery. In such cases, the obstetrician may attempt an external cephalic version. Otherwise delivery will be accomplished by cesarean section.

RETAINED PLACENTA

Retained placenta is defined as the retention of all or part of the placenta for more than 10 to 15 minutes after delivery of the infant.[15] It occurs in approximately 1% of all deliveries. If separation of the placenta does not occur within 15 minutes of delivery, manual removal is recommended.[15] Golan et al[24] suggested that intraumbilical vein administration of oxytocin is effective in the management of retained placenta, but this preliminary study did not include a control group. Three of four subsequent controlled studies have failed to demonstrate the efficacy of this technique.[10,33,44,53]

Occasionally, a large portion of the placenta separates and is delivered while a small portion remains within the uterus. A careful inspection of the placenta may alert the obstetrician to this occurrence. Otherwise a retained placental part may also be identified during manual exploration of the uterus after the third stage of labor. Infrequently, a patient leaves the delivery room with a portion of the placenta within the uterus. The obstetrician may be suspicious of this if post-delivery bleeding is excessive. Confirmation of the diagnosis and treatment require exploration of the uterus. Unfortunately, a significant period of time often elapses between delivery and uterine exploration. By the time the patient returns to the delivery room, she may be hypovolemic. Also, the cervix is likely to be contracted, making exploration difficult and painful. In some cases it is possible to strip away the retained placenta with forceps. This is not very painful and can often be performed without anesthesia. But the majority of women will require at least moderate levels of analgesia to tolerate the procedure.

Anesthetic Management of the Retained Placenta

If analgesia or anesthesia is required for removal of the retained placenta, the anesthesiologist should first evaluate the patient's volume and coagulation status. Tachycardia, flat neck veins, and orthostatic hypotension are suggestive of hypovolemia. In addition to the physical examination, the blood loss can be estimated by weighing the blood-soaked pads. Coagulation status can be evaluated by inspecting the vaginal blood for clots, examining intravenous catheter sites for oozing, and watching for clot formation within a red top tube. Formal coagulation studies (PT, PTT, fibrinogen, and platelet count) generally cannot be performed quickly enough to assist in the perioperative management of these patients.

Although analgesic drugs may be adequate for uterine exploration, particularly if the cervix remains dilated, care must be taken to avoid airway obstruction, respiratory depression, and loss of protective reflexes. For example, 40% nitrous oxide in oxygen can be administered. Intravenous narcotics (for example, fentanyl 25 to 100 μg, or alfentanil 250 to 1000 μg) are also effective. Ketamine is a potent analgesic; 10 to 20 mg may provide effective analgesia for up to 10 minutes. In contrast, benzodiazepines are not analgesics and have little or no role in management of the retained placenta except for their amnestic effects, which may last for several hours after their administration and interfere with maternal-infant bonding.

If a general anesthetic is given, the patient must still be regarded as having a full stomach and appropriate precautions must be taken to guard against regurgitation and aspiration. As stated previously, all the potent halogenated agents are equipotent uterine relaxants when given in equal anesthetic doses.[39] A high concentration of potent agent (for example 2 MAC) can be given until the retained placenta is removed. The potent agent should then be immediately discontinued to allow the uterus to contract and thus minimize further blood loss. The patient should remain anesthetized and intubated until exploration is complete, lacerations are repaired, and hemostasis is secured.

Regional anesthesia may be acceptable in selected cases. However, the anesthesiologist first must be certain that both the volume and coagulation status of the patient are acceptable. If an epidural catheter remains in place from labor and delivery, it can be reinjected. If an epidural catheter is not in place, then spinal or epidural anesthesia is acceptable. Because the sacral segments must be blocked to provide adequate anesthesia for uterine exploration, low spinal or caudal epidural anesthesia may be more reliable than lumbar epidural anesthesia. But it must be remembered that regional anesthesia does not provide uterine relaxation. If the obstetrician requests uterine relaxation, then general anesthesia with a potent halogenated agent is preferred.

Two preliminary reports suggested that intravenous nitroglycerine provides effective uterine relaxation for the manual removal of the retained placenta.[19,27] Unfortunately, neither study included a control group. Also, widely different doses of nitroglycerine were used (50 versus 500 μg). Although neither study reported adverse maternal hemodynamic effects, it is not clear how much bleeding had occurred before the nitroglycerine was given. Although it may be reasonable to try a small dose of nitroglycerine for relaxation of the uterus in the absence of maternal hypovolemia, it cannot be considered a standard or proven treatment at this time.

SUMMARY

Abnormal presentations complicate approximately 4% of all deliveries. The majority of these infants are in the breech presentation. Recent data suggest that vaginal delivery of the breech infant may be as safe as cesarean section. Epidural analgesia is preferred for vaginal delivery of the breech presentation. Sacral block may prevent premature maternal pushing and thus decrease the likelihood of cervical head entrapment. During delivery the obstetrician attempts to minimize trauma to the fetal head and neck. On occasion, general anesthesia is necessary to relieve cervical entrapment. The anesthesiologist should be prepared to administer general anesthesia to every patient with a breech presentation.

Multiple gestation complicates approximately 1 to 2% of all pregnancies. The physiologic changes of pregnancy are exaggerated with multiple gestation. For twin gestations, the presentation of the fetuses may influence the mode of delivery. Epidural analgesia is preferred for vaginal delivery. If a spontaneous delivery is planned, the motor block should be minimized. If internal podalic version and extraction of twin B is planned, epidural anesthesia alone may be sufficient. But, on occasion, general anesthesia is required for delivery of the second twin. Specifically, administration of a potent halogenated agent will relax the uterus and facilitate delivery of the second twin. For gestations of greater than two, delivery is generally performed via cesarean section. Either regional or general anesthesia is acceptable depending on the condition of the mother.

Shoulder dystocia occurs in up to 2% of vaginal deliveries. The dystocia is often relieved by changing the rotation of the maternal pelvis or changing the fetal position. Rarely, general anesthesia and skeletal muscle relaxation may be necessary. Following delivery the infant tends to be depressed and may require resuscitation. Rarely, the fetus cannot be delivered vaginally, is returned to the uterus, and delivered by cesarean section.

Retained placenta occurs in 1% of deliveries. Often there is significant blood loss with a retained placenta. Patients may require anesthesia for uterine exploration and removal of a retained placenta. General anesthesia with a potent halogenated agent provides cervical and uterine relaxation, which facilitates exploration. These patients must be considered to have a full stomach, and precautions must be taken to prevent against regurgitation and aspiration.

REFERENCES

1. Abouleish E: Caudal analgesia for quadruplet delivery. Anesth Analg 55:61–66 1976
2. American College of Obstetricians and Gynecologists Technical Bulletin: Management of the breech presentation, No. 95, 1986
3. American Society of Anesthesiologists: Standards for conduction anesthesia in obstetrics, 1988
4. Benedetti TJ, Gabbe SG: Shoulder dystocia—a complication of fetal macrosomia and prolonged second stage of labor with midpelvic delivery. Obstet Gynecol 52:526–529, 1978
5. Bevan DR, Holdcroft A, Loh L, et al: Closing volume and pregnancy. Br Med J 1:13–15, 1974
6. Bird CC, McElin TW: A six-year prospective study of term breech deliveries uti-

lizing the Zatuchni-Andros Prognostic Scoring Index. Am J Obstet Gynecol 121:551–558, 1975

7. Bowen-Simpkins P, Fergusson ILC: Lumbar epidural block and the breech presentation. Br J Anaesth 46:420–424, 1974
8. Brenner WE, Bruce RD, Hendricks CH: The characteristics and perils of breech presentation. Am J Obstet Gynecol 118:700–712, 1974
9. Chervenak FA, Johnson RE, Youcha S, et al: Intrapartum management of twin gestations. Obstet Gynecol 65:119–124, 1985
10. Chestnut DH, Wilcox LL: Influence of umbilical vein administration of oxytocin on the third stage of labor: A randomized, double-blind, placebo-controlled study. Am J Obstet Gynecol 157:160–162, 1987
11. Collea JV, Chein C, Quilligan EJ: The randomized management of term frank breech presentation: A study of 208 cases. Am J Obstet Gynecol 137:235–242, 1980
12. Collea JV, Rabin SC, Weghorst GR, et al: The randomized management of term frank breech presentation: Vaginal delivery vs. cesarean section. Am J Obstet Gynecol 131:186–195, 1978
13. Cohen M, Kohl SG, Rosenthal AH: Fetal interlocking complicating twin gestation. Am J Obstet Gynecol 91:407–412, 1965
14. Confino E, Ismajovich B, Rudick V, et al: Extradural analgesia in the management of singleton breech delivery. Br J Anaesth 57:892–895, 1985
15. Cotton DB: Abnormal labor and delivery. *In* Niswander KR: Manual of Obstetrics, ed 3. Boston, Little Brown, 1987, p 342
16. Crawford JS: An appraisal of lumbar epidural blockade in labour in patients with multiple pregnancy. Br J Obstet Gynecol 82:929–935, 1975
17. Crawford JS: An appraisal of lumbar epidural blockade in patients with singleton fetus presenting by the breech. J Obstet Gynaecol Br Comm. 81:867–872, 1974
18. Danforth DN: The distribution and functional activity of the cervical musculature. Am J Obstet Gynecol 68:1261–1271, 1954
19. DeSimone CA, Norris MC, Leighton BL, et al: Intravenous nitroglycerine for the manual extraction of a retained placenta (abstract). Proceedings of the annual meeting of the Society for Obstetric Anesthesia and Perinatology, San Francisco, California, 1988
20. Ekstein K, Marx G: Autocaval compression and uterine displacement. Anesthesiology 40:92–96, 1974
21. Fortunato SJ, Mercer LJ, Guzick S: External cephalic version with tocolysis: Factors associated with success. Obstet Gynecol 72:59–62, 1988
22. Gilstrap LC, Hauth JC, Hankins GDV, et al: Effect of type of anesthesia on blood loss at cesarean section. Obstet Gynecol 69:328–332, 1987
23. Gimovsky ML, Wallace RL, Schifrin BS, et al: Randomized management of the nonfrank breech presentation at term: A preliminary report. Am J Obstet Gynecol 146:34–40, 1983
24. Golan A, Lidor AL, Wexler S, et al: A new method for the management of the retained placenta. Am J Obstet Gynecol 146:708–709, 1983
25. Golditch IM, Kirkman K: The large fetus—management and outcome. Obstet Gynecol 52:26–30, 1978
26. Gonik B, Stringer CA, Held B: An alternate maneuver for management of shoulder dystocia. Am J Obstet Gynecol 145:882–884, 1983
27. Gorman R, Blancato L, Peng A, et al: Intravenous nitroglycerine for uterine relaxation (abstract). Anesthesiology 65:A392, 1988
28. Gross SJ, Shime J, Farine D: Shoulder dystocia: Predictors and outcome. Am J Obstet Gynecol 156:334–336, 1987
29. Guttmacher AF: The incidence of multiple births in man and some other unipara. Obstet Gynecol 2:22–35, 1953
30. Hendricks CH, Brenner WE: Cardiovascular effects of oxytocic drugs used postpartum. Am J Obstet Gynecol 108:751–760, 1970
31. James FM, Crawford JS, Davies P, et al: Lumbar epidural analgesia for labor and delivery of twins. Am J Obstet Gynecol 127:176–180, 1977
32. Kim YI, Chandra P, Marx GF: Successful management of severe aortocaval compression in twin pregnancy. Obstet Gynecol 46:362–364, 1975

33. Kristiansen FV, Frost L, Kaspersen P, et al: The effect of oxytocin injection into the umbilical vein for the management of the retained placenta. Am J Obstet Gynecol 156:979–980, 1987
34. Laros RK, Dattel BJ: Management of twin pregnancy: The vaginal route is still safe. Am J Obstet Gynecol 158:1330–1338, 1988
35. Little WA, Friedman E: The twin delivery—factors influencing second twin mortality. Obstet Gynecol Surv 13:611–623, 1958
36. Marx GF, Mateo CV: Effects of different oxygen concentrations during general anesthesia for elective caesarean section. Can Anaesth Soc J 18:587–593, 1971
37. Milner RDG: Neonatal mortality of breech deliveries with and without forceps to the aftercoming head. Br J Obstet Gynaecol 82:783–785, 1975
38. Morley GW: Breech presentation—a 15-year review. Obstet Gynecol 30:745–751, 1967
39. Munson ES, Embro WJ: Enflurane, isoflurane, and halothane and isolated human uterine muscle. Anesthesiology 46:11–14, 1977
40. Myers SA, Gleicher N: Breech delivery: Why the dilemma? Am J Obstet Gynecol 156:6–10, 1987
41. Norris MC, Dewan DM: Preoxygenation for cesarean section: A comparison of two techniques. Anesthesiology 62:827–829, 1985
42. Pritchard JA, MacDonald PC, Gant NF: Williams Obstetrics, ed 17. East Norwalk, Connecticut, Appleton-Century-Crofts, p 539
43. Rabinovici J, Barkai G, Reichman B, et al: Randomized management of the second nonvertex twin: Vaginal delivery or cesarean section? Am J Obstet Gynecol 156:52–56, 1987
44. Reddy VV, Carey JC: Effect of umbilical vein oxytocin on puerperal blood loss and length of third stage of labor. Am J Obstet Gynecol 160:206–208, 1989
45. Rovinsky JJ, Jaffin H: Cardiovascular hemodynamics in pregnancy. Am J Obstet Gynecol 93:1–15, 1965
46. Rovinsky JJ, Miller JA, Kaplan S: Management of breech presentation at term. Am J Obstet Gynecol 115:497–513, 1973
47. Sandberg EC: The Zavanelli maneuver extended: Progression of a revolutionary concept. Am J Obstet Gynecol 158:1347–1353, 1988
48. Seeds JW: Malpresentations. *In* Gabbe SG, Niebyl JR, Simpson JL (eds): Obstetrics: Normal and Problem Pregnancies. New York, Churchill Livingstone, 1986, p 476
49. Stine LE, Phelan JP, Wallace R, et al: Update on external cephalic version performed at term. Obstet Gynecol 65:642–646, 1985
50. Swartz DP: Shoulder girdle dystocia in vertex delivery. Obstet Gynecol 15:194–206, 1960
51. Thirion A-V, Wright RG, Messer CP, et al: Maternal blood loss associated with low dose halothane administration for cesarean section (abstract). Anesthesiology 69:A693, 1988
52. Warren TM, Datta S, Ostheimer GW, et al: Comparison of the maternal and neonatal effects of halothane, enflurane, and isoflurane for cesarean delivery. Anesth Analg 62:516–520, 1983
53. Young SB, Martelly PD, Greb L, et al: The effect of intra-umbilical oxytocin of the third stage of labor. Obstet Gynecol 71:736–738, 1988

Address reprint requests to

Kenneth L. Pollack, MD
Rockford Anesthesiologists Associated
2929 North Main Street
P.O. Box 1867
Rockford, IL 61110-0367

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Anesthesia for the Pregnant Patient Undergoing Nonobstetric Surgery

*Craig H. Leicht, MD, MPH**

It is not uncommon for a pregnant woman to undergo surgery for a nonobstetric indication sometime during her pregnancy. In the United States approximately 50,000 women per year, that is, 1.5 to 2% of pregnant women, receive an anesthetic for a surgical indication unrelated to delivery.[3, 17, 22] The commonest indications are appendectomy, breast biopsy, cervical cerclage, ovarian cystectomy, and increasingly, trauma. Other obstetric-related procedures in which anesthesia may be administered during pregnancy include intrauterine exchange transfusion and intrauterine fetal surgery. A procedure related to this topic, which deserves some mention, is in vitro fertilization. Undergoing a major neurosurgical or cardiac procedure while pregnant, although rare, is increasingly being reported.

Not unlike anesthesia administered for vaginal delivery and cesarean section, the physiologic changes of pregnancy pose additional considerations for the anesthesiologist and related risks to the mother and fetus alike. Additionally, because surgical procedures are performed at all ages of gestation, the fetus is frequently at risk for preterm labor or abortion, potential defects from teratogenic agents or therapies, hypoxia from perturbations of uterine blood flow, and from the disease process that necessitated the surgery.

ANESTHETIC CONSIDERATIONS IN GENERAL

The physiologic changes of pregnancy and potential adverse effects on the fetus must be considered in the administration of anesthesia or analgesia to the pregnant patient. Hormonal effects from the placenta and ovaries as well as mechanical effects of the gravid uterus are responsible for major changes in virtually all organ systems. It is

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* Director, Obstetric Anesthesia, U.S. Naval Hospital and Medical Center, San Diego, California

essential to understand these changes and their implications for anesthetic management to ensure the best possible outcome for mother and fetus undergoing surgery.

Maternal Considerations

Knowledge of the physiologic changes of pregnancy, and anesthetic considerations thereof, is the key to safeguarding the mother during anesthesia regardless of the specific procedure being performed. Therefore, in addition to being reviewed in other sections of this volume, the major physiologic changes of pregnancy and concomitant anesthetic considerations will be discussed here by each affected organ system.

Cardiovascular System. Changes in the cardiovascular system are indeed profound.[25, 26] Increases in cardiac output begin as early as 8 to 10 weeks gestation, approach a 35% increase by 20 weeks, reach their peak antepartum increase of 40 to 45% at 30 to 32 weeks, and slowly decline to an increase of 20% above the normal nonpregnant state at term. (The largest increase in cardiac output is about 60%, which occurs in the immediate postpartum period.) From as early as 20 weeks gestational age the gravid uterus may compress the vena cava and potentially partially occlude the descending aorta when the patient moves from lateral to supine position; thus producing abrupt drops in cardiac output from the usual increased values of pregnancy to below that of the normal nonpregnant state. Therefore, care must be taken to avoid a totally supine position. Utilization of left lateral tilt or hip roll is an absolute necessity even early in gestation. This is true for local, regional, and general anesthesia alike. Additionally, pregnant patients normally may exhibit electrocardiographic changes and murmurs not normally present in the nonpregnant state that may not be easily distinguished from true pathologic changes in some circumstances.

Respiratory System. A 60 to 70% increase in alveolar ventilation, a 15% increase in respiratory rate, and a 40% increase in tidal volume explain the decrease in maternal Pa_{CO_2} to approximately 32 torr.[2, 8, 18] This also contributes to a more rapid induction and emergence from inhalation anesthetics. This physiologic hyperventilation also explains the near normal or slightly increased Pa_{O_2} in spite of increased oxygen consumption in pregnancy. However, most significant is the increased risk of the rapid development of hypoxia and acidosis; a 20% decrease in functional residual capacity (FRC) combined with increases in basal metabolic rate and oxygen consumption are the predominant factors. Therefore, adequate time for preoxygenation must be assured. Enlarged breasts and engorged respiratory tract mucosa may contribute to the difficulty with ventilation and intubation of these patients. Likewise, the glottic opening may be narrowed due to edema, necessitating a smaller endotracheal tube (6.5 or 7.0 mm outside diameter). Pregnant patients undergoing procedures under local or regional anesthesia should also receive supplemental oxygen.

Central Nervous System. The minimal alveolar concentration

(MAC) of all commonly used inhalation agents is decreased by 25 to 40% in pregnancy.[12, 16] Pregnant patients experience a more rapid onset and a higher level of spinal or epidural anesthesia compared with age-matched nonpregnant controls given the same dose of local anesthetic. Therefore, all drugs, that is, local anesthetic agents, narcotics, sedatives, and inhalation anesthetic agents, should be titrated to effect whenever possible.

Renal System. Glomerular filtration rate and renal blood flow both increase significantly in pregnancy and may alter the pharmacokinetics/dynamics of many drugs, especially those excreted by the kidneys.[6]

Gastrointestinal System. The hormonal and mechanical changes of pregnancy account for a decrease in lower esophageal sphincter tone, a decrease in gastric motility, an increase in intragastric pressure, increases in gastric secretion and acidity, and outflow obstruction, which places the pregnant patient at very high risk for aspiration of gastric contents.[13, 19] Some of these changes occur very early in gestation and therefore maneuvers to decrease the risk of aspiration should be employed in all pregnant patients. As a general rule, the following simple measures should be used for all pregnant patients undergoing general anesthesia: a clear oral antacid should be administered preoperatively, cricoid pressure should be applied during the induction of anesthesia, the trachea of the pregnant patient should be routinely intubated, and extubation of the trachea should be performed only after the patient is fully awake. A clear oral antacid should also be administered preoperatively to pregnant patients undergoing procedures under regional or local anesthesia.

Hematologic System. A 20% increase in red blood cell volume with a concomitant 40 to 50% increase in plasma volume accounts for the so-called "physiologic anemia of pregnancy."[9, 23] Plasma proteins are likewise diluted and may affect the pharmacokinetics of highly protein-bound drugs. Plasma cholinesterase levels inversely decrease as gestation increases. This is probably secondary to decreases in production as well as a dilutional effect. Fortunately, under normal conditions, the clinical effect is usually insignificant. Increased levels of fibrinogen and other clotting factors lead to a hypercoagulable state that increases the risk of thromboembolic complications.

Fetal Considerations

In general, with regard to the fetus, there are three main areas of concern: (1) maintenance of fetal oxygenation; (2) avoidance of teratogenic agents; and (3) prevention of preterm labor.

Maintenance of Fetal Oxygenation. Maintenance of fetal oxygenation is dependent on the ability to maintain both maternal oxygen content and intervillous blood flow. This requires maintenance of normal maternal PaO_2 and $PaCO_2$, maternal blood pressure, and uterine vascular resistance. For the most part, the causes and treatment of maternal hypoxemia under general anesthesia are the same as for any ventilated patient with the addition of the parturient's propensity for rapid desaturation. There is no reason to avoid the administration of high concentrations of oxygen to the mother as maternal hyperoxia presents no risk to the fetus. Even with a maternal $\mathrm{PaO_2}$ of 600 torr, the fetal $\mathrm{PaO_2}$ does not rise above 50 to 60 torr. There is, therefore, no risk of retrolental fibroplasia or premature closure of the ductus arteriosus in utero secondary to increased maternal oxygen content.

The baseline state of the uterine vasculature is wide dilation with little capability to dilate further. However, the uterine vasculature is capable of marked constriction. Hyperventilation, that is, maternal alkalosis, will reduce intervillous blood flow by causing direct vasocontriction. Additionally, this will increase the affinity of maternal hemoglobin for oxygen, resulting in a decrease in release of oxygen to the fetus in the intervillous space. Direct-acting vasoconstrictors, that is, alpha-agents, such as phenylephrine, will cause uterine vasoconstriction and decreased intervillous blood flow. (Ephedrine, an indirect acting agent, is the recommended drug for maternal hypotension.) Maternal hypercapnia will produce respiratory acidosis in the fetus. Excessive positive-pressure ventilation may increase intrathoracic pressure, decrease venous return, and decrease cardiac output, thereby causing a decrease in uterine blood flow. Uterine arterial blood flow is directly dependent on maternal blood pressure. A decrease in maternal blood pressure will cause a decrease in uterine blood flow, a decrease in intervillous blood flow, and eventually fetal asphyxia. Deep levels of inhalation agents will cause maternal hypotension and resultant fetal asphyxia. However, with lighter levels of these agents, the decrease in maternal blood pressure is minimal. At levels of general anesthesia sufficient to attenuate the stress response to surgery, but not sufficiently deep as to significantly decrease maternal blood pressure, uterine vascular resistance may actually slightly decrease and intervillous blood flow slightly improve. However, this relationship is tenuous at best and, therefore, maintenance of maternal blood pressure must be considered the highest priority, as it is measurable and treatable. Maternal hypotension must be avoided, if at all possible, and treated promptly if it occurs. Treatment should consist of intravenous fluid administration, repositioning the patient to a more lateral position, if at all possible, decreasing the anesthetic concentration, and administration of an appropriate vasopressor (ephedrine), if necessary. Additionally, repositioning of surgical packs and retractors should be considered, as the combination of poorly positioned packs and retractors and a gravid uterus may lead to hypotension refractory to all other modes of therapy. Whenever possible, fetal heart tones should be monitored in the intraoperative and early postoperative periods.

Avoidance of Teratogenic Agents. Many premedicants and anesthetics are teratogenic in some animal species under some conditions. Furthermore, certain conditions in the absence of medications or anesthetics, such as hyperbaric oxygen, hypoxia, and hypercapnia may also be teratogenic in some animals. There are many factors that may determine whether or not an agent will be teratogenic in humans.

These include (1) dose and duration of exposure, (2) the embryonic/fetal stage at which the agent is administered, and (3) species-specific genetic susceptibility to the agent. It is apparent, therefore, that a drug that may cause a defect in animal studies may not necessarily be teratogenic in man. Also, the finding of teratogenesis after exposure to very high doses, or prolonged chronic exposure at lower doses, does not mean that a single short exposure during the course of an anesthetic would likewise cause a defect. There may be sensitivity to exposure during certain stages of development and little or no effect at a different time. Generally speaking, the most critical stage of development is thought to be during the period of organogenesis at 15 to 56 days gestation. There also may be a particular sensitivity of the central nervous system to external factors at a later time, specifically during the period of myelination, which is thought to extend from late second trimester to a few days after birth.

Of the anesthetic agents commonly used in pregnancy, nitrous oxide (N_2O) has received the most attention recently. The potential toxic effects of N_2O appear to be related to its capacity to inactivate an enzyme, methionine synthetase. Methionine synthetase is responsible for the conversion of homocystiene and methyltetrahydrofolate to methionine and tetrahydrofolate. Methionine is an essential amino acid whereas tetrahydrofolate is needed for the synthesis of DNA. The inactivation of methionine synthetase persists for several days in animals given N_2O. The inactivation of methionine synthetase appears to occur in both the mother and the fetus.[15] This effect has not been proved to be clinically significant in humans. It has been suggested that folinic acid, methionine, and vitamin B_{12} be administered to pregnant patients undergoing anesthesia with N_2O in an attempt to prevent this potential problem; however, this has not yet been proved clinically effective. It is our practice, because of the previously mentioned theoretical concerns, to simply avoid the administration of N_2O to pregnant patients whenever possible, especially in the first trimester.

Teratogenicity: Human Studies and Implications. Shnider and Webster[22] reviewed the records of over 9000 obstetric patients of whom 1.6% underwent surgery during pregnancy. Premature delivery occurred in 9% (7.5% perinatal mortality) compared with 2.2% of those who did not undergo surgery. Duncan et al[7] surveyed health insurance data of the entire Manitoba population over an 8-year period. During that time, over 2500 women who underwent surgery during pregnancy were matched with pregnant controls who did not undergo surgery. Again the incidence of spontaneous abortion was increased in the patients who underwent surgery during pregnancy, being the highest for those patients undergoing gynecologic surgery during pregnancy. However, the incidence of congenital anomalies was similar in surgery and control groups. Brodsky et al[3] reviewed the fetal outcome of 287 women who underwent surgery during pregnancy. These authors also found that surgery during early pregnancy was associated with a significant increase in the rate of spontaneous abortion compared with the control group (no surgery during pregnancy), but there were no differences in the incidence of congenital anomalies in the offspring of the women between the groups. None of these or other studies have shown an increase in congenital anomalies secondary to anesthesia for surgery during pregnancy in humans. It is interesting to note that the Swedish Catalogue of Registered Pharmaceutical Specialists has classified anesthetic agents in category A; that is, no known teratogenicity. In contrast, there is some evidence that the hospitalized pregnant patient is exposed to a number of environmental and chemical factors that are potentially teratogenic. These include emotional stress, confinement to a hospital bed, hypoglycemia, irradiation, aminoglycoside antibiotics, warfarin anticoagulants, and antiepileptic drugs.

Although it appears that surgery during pregnancy is associated with an increased incidence of spontaneous abortion and fetal demise, there is no evidence that this increase is associated with anesthesia per se. Rather, the increased fetal loss appears to be associated with the procedure itself, the site of the surgery, or the underlying condition that necessitated the surgery. Finally, there is no clinical evidence that a particular type of anesthetic is associated with a better outcome than any other type of anesthetic for surgery during pregnancy, provided maternal blood pressure, oxygenation, and homeostasis is maintained.

Prevention of Preterm Labor. As noted in the preceding discussion of teratogenicity, Brodsky,[3] Shnider,[23] and Duncan[7] all found the incidence of preterm labor and spontaneous abortion to be markedly increased in patients who underwent surgery during pregnancy. Therefore, it is critical that uterine activity be monitored closely during surgery and in the immediate postoperative period, and treatment instituted promptly if uterine contractions develop. Some obstetricians prefer to use prophylactic tocolysis to prevent preterm labor in patients who appear to be at significant risk for developing such during surgery; however, clinical studies have not documented its efficacy. Unfortunately, no ideal agent for tocolysis exists currently. The most commonly used therapeutic agents are β-adrenergic agonists (ritrodrine and terbutaline) and magnesium sulfate, although many other agents have been used for this purpose. Each of these agents have potential maternal and fetal side effects and concomitant anesthetic implications. Most notorious are the β-adrenergic agonists; reported side effects thereof include hypokalemia, hyperglycemia, pulmonary edema, tachycardia, premature ventricular contractions (PVCs), chest tightness, myocardial ischemia, ST-segment and T-wave changes on the ECG, atrial fibrillation, and rarely, maternal death associated with unrecognized heart disease. The tachycardia, which is almost universally present, makes it difficult to estimate the level of anesthesia and fluid status. Because of the increased risk of dysrhythmias, sympathomimetic agents such as ephedrine, halothane, ketamine, and pancuronium should be used with caution. Atropine and glycopyrrolate should be avoided as well. Also, hyperventilation should be avoided, as this will further increase the intracellular movement of potassium. Because of the increased risk of pulmonary edema the patient's fluid status must be carefully evaluated. This is especially true prior to prehydration for regional anesthesia. Minimal prehydration is recommended, and if hypotension develops, small boluses of fluids and ephedrine should be administered with caution.

Magnesium sulfate is the other frequently used tocolytic agent and offers the advantage of generally fewer maternal and fetal side effects. Magnesium is excreted solely by the kidneys, and therefore, renal impairment is a relative contraindication. Its mechanism of action is not entirely understood. However, it is a smooth muscle relaxant as well as a depressant of neuromuscular conduction. It probably prevents the increase in intracellular calcium concentration that is necessary for muscle contraction by competing with calcium for surface-binding sites on the smooth muscle. Magnesium also acts at the neuromuscular junction; presynaptically, by decreasing the release of acetylcholine and, postsynaptically, by decreasing the sensitivity of the endplate to acetylcholine. Patients being administered magnesium sulfate are, therefore, more sensitive to both depolarizing and nondepolarizing muscle relaxants. It is not necessary and may be dangerous to pretreat with a nondepolarizing agent prior to the administration of succinylcholine. It is our practice to give our usual dose of muscle relaxant for intubation, being well aware that the duration may be prolonged. Additional doses of muscle relaxants should be titrated to effect using a neuromuscular blockade monitor. Toxic doses of magnesium sulfate may have profound depressive effects on cardiac and respiratory function. Therefore, a baseline magnesium sulfate level should be obtained prior to proceeding with the anesthetic. If necessary, many of the toxic effects of magnesium can be reversed by the judicious administration of calcium.

Patients prophylatically treated with a tocolytic agent should have the agent continued 24 to 48 hours postoperatively. All patients should be monitored postoperatively for the presence of uterine contractions. If regular uterine contractions are present, especially in light of a change in cervical examination, tocolysis, at full therapeutic doses, should be considered. Other diagnostic measures must also be undertaken to rule out other causes of premature labor, such as chorioamnionitis, urinary tract infection, and abruptio placentae.

Implications of Adjuvant Therapies Common to Anesthetic Practice

Controlled Hypotension. Controlled hypotension should not be routinely used as an adjunct to anesthesia for surgery in a pregnant patient. However, there may be certain circumstances that warrant its use; for example, in a craniotomy on a pregnant woman for repair of a vascular lesion. In this case, inducing controlled hypotension will reduce the likelihood of rupture of the lesion, but may also cause fetal asphyxia. Hypotensive anesthesia has reportedly been successfully used in some such cases,[14] whereas in other cases fetal distress or death has resulted.[20] The drugs commonly used include halogenated anesthetic agents, sodium nitroprusside, nitroglycerin, and trimethaphan. The use of halogenated agents for this purpose is probably contraindicated, because high concentrations of these agents cause depressed myocardial contractility resulting in significant maternal hypotension causing decreased uterine blood flow and fetal asphyxia. Sodium nitroprusside is a very effective and titratable agent for controlled hypotension. However, it rapidly crosses the placenta and is degraded to cyanogen, which is potentially toxic to the fetus. Its use in pregnancy should probably be limited to small doses and short periods of time. Nitroglycerin, our first choice for this indication, although slower in onset than nitroprusside, is essentially nontoxic to the fetus and has been shown to be effective in the sheep model.[27] Trimethaphan is a ganglionic blocking agent whose hypotensive effect depends primarily on the venous pooling of blood, which decreases venous return to the heart and thereby decreases cardiac output. This drug also reduces the pregnant patient's normal response to caval compression, prolongs the action of succinylcholine by inhibiting plasma pseudocholinesterases, and causes dilation of the pupils, which may impair neurologic assessment of the patient.

When induced hypotension is necessary, the drop in maternal blood pressure should be limited in extent and duration to the minimum required for the case. Maternal arterial pH should be measured frequently to avoid risks of severe fetal or maternal compromise and the fetal heart rate must be monitored closely throughout the case.

Osmotic Diuretics. Osmotic diuretics such as mannitol and urea are typically used in neurosurgical procedures to reduce cerebral edema. Unfortunately, these agents can cause a net flow of water away from the fetus to the mother.[4] This is of little consequence to the mother, but in the fetus may cause severe dehydration, and therefore, should be used only if absolutely necessary during pregnancy.

Hypothermia. Hypothermia has been used as an adjunct to anesthesia in certain cardiac and neurosurgical procedures in an attempt to reduce metabolic requirement for oxygen. Moderate hypothermia, 30 ± 2°C, has been successfully used as an adjunct to anesthesia for surgery during pregnancy.[24] Intervillous blood flow decreases secondary to increased uterine vascular resistance, but oxygen transport remains unaffected. The fetus also becomes hypothermic and its metabolic needs will proportionally decrease. As long as maternal blood gas and acid base status is optimized, the fetus should tolerate moderate hypothermia.

Hyperventilation and Hypocapnia. Recalling that the maternal $Paco_2$ is normally 32 mm Hg, with a pH of 7.40 to 7.45, the anesthesiologist should strive to maintain these values throughout surgery. Extreme hyperventilation will cause decreases in uterine blood flow, placental oxygen transport, and fetal Po_2, resulting in fetal hypoxia and acidosis. However, mild hyperventilation, that is, decreases of 5 to 7 torr, may be tolerated by the fetus. This course should be undertaken only with a fetal heart rate monitor in place, and with the understanding that ventilation will be returned to normal if signs of fetal distress appear on the monitor. The use of hyperventilation in a pregnant patient should be limited in extent and duration and should be reserved for cases in which there is a proven need for its utilization.

Specific Circumstances

Anesthesia for Fetal Surgery. A variety of interventions, most commonly intrauterine exchange transfusion, but also antenatal placement of diversion catheters and aspiration of fetal cystic masses, are being performed with increased frequency. These procedures are usually performed on an "awake" patient under a combination of maternal sedation/analgesia and local anesthesia.

In the past, heavy sedation, for example, moderate to high doses of diazepam, was administered to the mother in an attempt to sedate the mother and fetus and help decrease fetal movement. More recently, the use of a nondepolarizing muscle relaxant administered intramuscularly or intravenously to the fetus has been used to decrease fetal movement. Pancuronium 0.5 mg[21] and D-tubocurare 3 mg per kg[5] administered intramuscularly and atracurium 0.4 mg per kg[1] administered intravenously have been described to successfully arrest fetal movement with no apparent maternal or fetal side effects. The duration of intramuscular pancuronium or D-tubocurare is 2 to 4 hours and 30 to 60 minutes for intravenous atracurium. The use of fetal intramuscular or intravenous muscle relaxants eliminates the need for excessive maternal sedation. A potential advantage of the use of the intravenous route over the intramuscular route is the avoidance of injection of the drug into the fetal thigh, which could potentially result in nerve damage or hematoma formation. Because both pancuronium and D-tubocurare are both largely metabolized in the liver and because severely erythroblastotic fetuses have significant hepatic impairment; atracurium, because of its alternative pathway of elimination, may be a reasonable choice for muscle relaxation in this situation.

Our current practice is to administer midazolam 1 to 2 mg and fentanyl 50 to 100 μg intravenously to provide mild sedation/analgesia for the mother. The obstetrician then administers local anesthesia to the abdomen in a fashion similar to that for amniocentesis. This is followed by injection of 0.4 mg per kg of atracurium into the umbilical vein of the fetus, which results in almost immediate cessation of fetal movement lasting for 30 to 60 minutes. We have been satisfied that this combination has provided comfort to the mother and optimum operating conditions for the surgeon while avoiding excessive maternal sedation.

Anesthesia for In Vitro Fertilization. The technique of in vitro fertilization with embryo transfer is now being widely used to treat infertile couples. Although the method was originally restricted to women who had no functioning oviducts as a result of severe tubal disease, it is now being used in cases of severe endometriosis and couples with "male factor" or unexplained infertility. Until recently, laparoscopy has been the most widely used method for oocyte collection in in vitro fertilization. In the last few years ultrasonically guided oocyte collection has been introduced in an increasing number of in vitro fertilization centers.[11] Ultrasonically guided oocyte collection may be performed transabdominally, transvesically, or transvaginally. With the change in method of oocyte retrieval, the anesthetic requirement for the procedure has changed as well. In most cases, when ultrasonically guided oocyte collection is used, an anesthesiologist's services are no longer required. Local anesthesia with mild sedation is usually employed by the obstetrician.

In centers where laparoscopy is still in use, an anesthetic is required as for any laparoscopic procedure. Both general and regional anesthesia have been employed for laparoscopic oocyte retrieval. Our bias is to use epidural anesthesia for these cases whenever possible. However, for regional anesthesia to be successfully employed, the surgeon must learn to insufflate less CO_2 and use Trendelenburg's position less frequently than employed in many laparoscopic procedures. Our choice is based on the theoretical concern of the possible effect(s) on the oocyte of higher systemic levels of multiple anesthetic agents that accompany general anesthesia. There is some evidence that general anesthesia may change the concentration of certain regulatory peptides found in follicular fluid.[10] Furthermore, many of these patients undergo multiple procedures in a relatively short period of time. However, at this time there is no outcome data to support either type of anesthetic as being superior over the other type with regard to clinical pregnancy rate or difference in incidence of malformations.

SUMMARY

There are, therefore, a multitude of concerns that require consideration with regard to providing anesthesia care for the pregnant patient undergoing surgery. However, the basic considerations common to all such cases are the following: (1) The physiologic changes of pregnancy must be understood and the anesthetic implications thereof must be acted upon. (2) Maternal blood pressure and uteroplacental perfusion must be maintained. Hypotension and aortocaval compression should be avoided; however, if these should occur, treatment should be instituted promptly. (3) Anesthetic techniques should be selected that limit the exposure of mother and fetus to potentially teratogenic agents; remembering, however, that no anesthetic agent has yet been proved to be teratogenic in man. Regional anesthesia should be used whenever possible. (4) Preoperatively, discuss with the patient the implications of surgery and anesthesia during pregnancy, including our current knowledge regarding the lack of known teratogenicity of anesthetic agents. (5) Fetal heart rate and uterine activity should be monitored intraoperatively and postoperatively; if changes are noted, the anesthetic technique should be modified accordingly.

REFERENCES

1. Berkowitz RL, Chitkara U, Wilkins IA, et al: Intervascular monitoring and management of erythroblastosis fetalis. Am J Obstet Gynecol 158:783–795, 1988
2. Bonica JJ: Maternal respiratory changes during pregnancy and parturition. *In* Marx G (ed): Parturition and Perinatology. Clinical Anesthesia Series, Vol. 10, No. 2. Philadelphia, Davis, 1973, p 9
3. Brodsky JB, Cohen EM, Brown BW, et al: Surgery during pregnancy and fetal outcome. Am J Obstet Gynecol 138:1165, 1980
4. Bruns PD, Linder RO, Drose VE, et al: The placental transfer of water from fetus to mother following the intravenous infusion of hypertonic mannitol to the maternal rabbit. Am J Obstet Gynecol 86:160–167, 1963
5. de Crespigny LC, Robinson HP, Quinn M, et al: Ultrasound guided fetal blood transfusion for severe Rhesus isoimmunization. Obstet Gynecol 66:529–532, 1985
6. Digman WJ, Titus P, Assali NS: Renal function in human pregnancy. Proc Soc Exp Biol Med 97:512–514, 1958
7. Duncan PG, Pope WDB, Cohen MM, et al: Fetal risk of anesthesia and surgery during pregnancy. Anesthesiology 64:790, 1986
8. Gee JBL, Packer BS, Miller JE: Pulmonary mechanics during pregnancy. J Clin Invest 46:945–952, 1967
9. Hathaway WE, Bonnar J: Coagulation in pregnancy. *In* Hathaway WE, Bonnars J (eds): Perinatal Coagulation. Philadelphia, Grune & Stratton, 1978
10. Jarry H, Meyr B, Holzapel G, et al: Angiotensin II/III and substance P in human follicular fluid obtained during IVF. Acta Endocrinol 119:277–282, 1988
11. Lewin A, Laufer N, Rabinowitz R, et al: Ultrasonically guided oocyte collection under local anesthesia: The first choice method for in vitro fertilization—a comparative study with laparoscopy. Fertil Steril 46:257–216, 1986
12. Marx GF: Regional anesthesia in obstetrics. Anaesthetist 21:84–91, 1972
13. Marx GF: Physiology of pregnancy. *In* Hershey SC (ed): ASA Refresher Courses in Anesthesiology, Vol 3. Philadelphia, Lippincott, 1975, pp 117–128
14. Minielly R, Yupze AA, Drake CG: Subarachnoid hemorrhage secondary to ruptured cerebral aneurysm in pregnancy. Obstet Gynecol 53:64–70, 1979
15. Nunn JF, Chanarin I: Nitrous oxide inactivates methionine synthetase. *In* Eger EI II (ed): Nitrous Oxide/N_2O. New York, Elsevier, 1985
16. Palaniuk RJ, Shnider SM, Eger EI II: Pregnancy decreases the requirement for inhaled anesthetic agents. Anesthesiology 41:82–83, 1974
17. Pedersen H, Finster M: Anesthetic risk in the pregnant surgical patient. Anesthesiology 51:439, 1979
18. Prowse CM, Caensler EA: Respiratory acid base changes during pregnancy. Anesthesiology 26:381–392, 1965
19. Roberts RB, Shirley MB: Reducing the risk of acid aspiration during ceserean section. Anesth Analg 53:859–868, 1974
20. Robinson JL, Chir B, Hall CJ, et al: Subarachnoid hemorrhage in pregnancy. J Neurosurg 37:27–33, 1972
21. Seeds JW, Coorke BC, Spielman FJ: Prevention of fetal movement during invasive procedures with pancuronium bromide. Am J Obstet Gynecol 155:818–819, 1986
22. Shnider SM, Webster GM: Maternal and fetal hazards of surgery during pregnancy. Am J Obstet Gynecol 92:891–900, 1965
23. Shnider SM: Serum cholinesterase activity during pregnancy. Anesthesiology 26:335–339, 1965
24. Stange K, Halldin M: Hypothermia in pregnancy. Anesthesiology 58:460–461, 1983

25. Ueland K, Hansen J: Maternal cardiovascular hemodynamics II and III. Am J Obstet Gynecol 103:1–18, 1969
26. Ueland K, Novy M, Peterson E, et al: Maternal cardiovascular hemodynamics IV. Am J Obstet Gynecol 104:156–164, 1969
27. Wheeler AS, James FM III, Meis PJ, et al: Effects of nitroglycerin and nitroprusside on the uterine vasculature of gravid ewes. Anesthesiology 52:390–394, 1980

Address reprint requests to

Craig H. Leicht, MD, MPH
Director, Obstetric Anesthesia
U.S. Naval Hospital and Medical Center
San Diego, CA 92134

Anesthesia for Postpartum Complications

*Walter L. Millar, MD**

The majority of postpartum complications requiring an anesthesiologist's participation involve bleeding. This article reviews the more common problems and the anesthetic considerations associated with them. Postpartum hemorrhage may present the anesthesiologist with a confusing clinical situation, without prior warning and with great urgency for treatment. Significant but self-limited bleeding is incidental to normal delivery. Excessive or ongoing bleeding may be difficult to recognize or quantitate, and dilatory treatment usually does not produce morbidity, because the parturient is capable of remarkable physiologic adaptation to blood loss. Although it is rare, uncontrolled postpartum hemorrhage is still a major cause of maternal death in North America[9, 10]; the vast majority of such deaths are preventable.

The anesthesiologist's tasks are to assess the severity of the hemorrhage, to provide appropriate volume resuscitation, and to provide optimal operating conditions for what may be a series of obstetric interventions, without exposing the patient to unnecessary additional risk. These tasks may have to be done in a site remote from the familiar environment of the operating suite, at any time of the day or night. Understanding the pathophysiology of obstetric hemorrhage, prior preparation, and anticipating the obstetrician's diagnostic and therapeutic maneuvers are essential to providing optimum anesthetic care. This article is intended to assist the occasional obstetric anesthesiologist to prepare for this situation.

MECHANISM OF NORMAL OBSTETRIC HEMOSTASIS

The human placenta is perfused by 100 to 200 spiral arterioles, fed by an anastomotic network derived from the paired uterine and ovar-

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* Associate Clinical Professor of Anesthesiology, University of California, San Diego; Staff Anesthesiologist, Anesthesia Service Medical Group, Inc., San Diego, California

ian arteries, which empty into the intervillous space. The blood in the intervillous space bathes the chorion of the fetal villi, across which exchange of oxygen and other substrates occurs, and it empties into venous sinuses in the basal plate of the placenta. When the placenta separates following delivery, the spiral arterioles are briefly left to empty directly into the uterine cavity. Normally, total flow almost instantaneously decreases, from 600 to 900 mL per minute to virtually zero. As a consequence, blood loss during normal vaginal delivery averages only 500 to 600 mL, most of it blood already contained in the intervillous space when separation occurred.

Contraction of the uterus accomplishes this diminution of flow by compressing and kinking the spiral arterioles as they course through the contracted myometrium. This amazingly efficient mechanism of obstetric hemostasis is mechanical ("physiologic ligatures"). It is effective, even in the patient with a complete inability of the blood to clot, although the patient with a bleeding diathesis may develop hemorrhage from minor tears of the birth canal. During cesarean section, average blood loss increases to 1000 to 1200 mL, because the uterus may not contract physiologically and because of bleeding related to hysterotomy.

Following cessation of flow in the spiral arterioles, a platelet plug forms, leading to activation of the clotting cascade and formation of a fibrin clot. Sustained contraction of the uterus following delivery, stimulated by endogenous or exogenous oxytocin, allows this stable clot to form. If the primary mechanism (mechanical occlusion) of hemostasis fails, a platelet plug and clot may still form if arteriolar flow is sufficiently reduced, either by hypotension or by therapeutic occlusion of the arterial supply.

The healthy parturient is prepared for the normal 500-mL blood loss by the physiologic changes of pregnancy. Increases in plasma volume and red cell mass are accomodated by increased venous compliance, so that the parturient at term has a large blood volume reservoir in the capacitance system. Physical and neuroendocrine adaptations to hypovolemia are readily activated, such as mobilization of extracellular fluid (also increased), sympathetic arousal, and vasoconstriction. Because of these adaptations, blood loss several times that usually resulting from vaginal delivery is tolerated without serious sequelae. Postpartum hemorrhage is defined as blood loss exceeding 500 mL for vaginal delivery, or any significant hemorrhage following cesarean section.

MECHANISM OF FAILED OBSTETRIC HEMOSTASIS

Postpartum uterine bleeding most often results from impaired contraction of the myometrium underlying the placental implantation. Global uterine atony is the most common cause. The pathophysiology of atony at the cellular level is not well defined, but overstretching of the contractile fibers and depletion of high-energy phosphate stores are contributing factors. The clinical associations are with uterine distension by multiple pregnancy, polyhydramnios, or fetal macrosomia, prolonged or oxytocin-stimulated labor, grand multiparity, and sepsis. Although global atony is the most common cause, it is a diagnosis of exclusion, because other causes require specific treatment.

Generalized failure of myometrial contraction may also occur if the normally contractile uterus is distended by placenta or blood. Localized failure may occur if a placental fragment or succenturiate lobe is retained, if the placenta has implanted on the cervix or lower uterine segment, which are poorly contractile (usually in conjunction with placenta previa), if abnormal placental implantation has invaded myometrium (placenta accreta), or if intramyometrial hematoma has formed (Couvelaire uterus). A special case of localized failure is uterine inversion; the fundus cannot effectively contract because it is turned inside out, while contraction of the lower uterine segment serves to entrap the inverted fundus.

EXTRAUTERINE SOURCES OF OBSTETRIC HEMORRHAGE

The forces of uterine contraction during labor result in fundal thickening, effacement of the cervix, and progressive dilatation of the cervix, vagina, and introitus as delivery progresses. Estrogen and progesterone alter the connective tissue ultrastructure of the birth canal, so that expulsion of the fetus usually is accomplished with minimal tearing. Fetal macrosomia, dead fetus, precipitous labor, prior scarring, and obstetric forceps are associated with more extensive trauma. Major, life-threatening hemorrhage may occur in the case of rupture of the corpus uteri or laceration of the cervix that extends into the peritoneum, broad ligament, or retroperitoneal space. Perineal bleeding may be insidious, for the loose paravaginal tissues may allow several units of blood to accumulate without external evidence of bleeding.

PREPARATION FOR POSTPARTUM COMPLICATIONS

An operating room capable of accommodating major surgery must be available to the obstetric suite. In addition to the basic anesthesia machine and monitors, the anesthesiologist should have ready access to electronic pressure transducers, specialized equipment for rapid infusion of intravenous fluids, and devices that warm these fluids. Resuscitation in an environment where exsanguinating hemorrhage rarely occurs requires additional personnel, so that a plan for emergency communication via telephone, intercom, or pager should be set out in advance, utilizing whatever hospital administrative resources are available.

Consultation with the hospital blood bank allows the planning of a "massive transfusion protocol," facilitating access to regional blood banks and promoting efficiency in the delivery of hospital bank blood when the need arises.

If the obstetric operating room is not in the main operating room area, it is useful to keep a cart or tray stacked with large-bore intravenous tubing, blood filters and pumps, catheters for venous and arterial cannulation, blood warmer inserts, and central venous cannulation trays and manometers. A supply of pre-warmed (37 to 40°C) balanced salt solution for intravenous infusion is invaluable in preventing hypothermia during fluid resuscitation; warm fluid also prevents shivering and discomfort in routine administration to patients in labor.

Postpartum hemorrhage usually occurs during the first hour following delivery, sometimes termed the fourth stage of labor. Because an indwelling epidural catheter is so convenient for safely producing complete analgesia, removal of labor epidural catheters is best delayed until after this fourth stage. Because of the time required for positioning, epidural puncture, administration of test dose, and latency of the local anesthetic, it is seldom worthwhile to initiate epidural anesthesia de novo for this procedure.

TREATMENT OF POSTPARTUM HEMORRHAGE

When obstetric hemorrhage warrants intervention, the patient should be moved to the operating room for monitoring and definitive diagnosis and therapy. Administrative and nursing help for the anesthesiologist should be enlisted early, because the solo anesthesiologist, once engaged in care of the patient, may be unable to coordinate the effort of obtaining necessary additional services and equipment. A plan of management based on the patient's history, clinical course, and preexistent medical problems should be decided upon between obstetrician, anesthesiologist, and nurses.

Certain initial resuscitative maneuvers—basic life support, application of monitors, venous cannulation—should be familiar to all members of the obstetric team, so that they may be begun prior to the anesthesiologist's arrival. The first priority is to assure adequate ventilation. The patient who is comatose or apneic requires immediate mask ventilation with 100% oxygen with the application of cricoid pressure and eventual endotracheal intubation and mechanical ventilation. The patient who is awake and able to speak may breathe supplemental oxygen from a mask or nasal prongs while assessment continues. A pulse oximeter should be applied to provide real-time assessment of arterial oxygen saturation and an indirect monitor of the adequacy of the peripheral pulse.

Circulation is the next priority. The patient's initial positioning should be supine, tilted head down (Trendelenburg's position) to promote venous return. Blood pressure should be measured and recorded, recognizing that a normal pressure may be present even with moderate hypovolemia. Venous access must be secured as expeditiously as possible with the largest intravenous cannula practical. The dilated capacitance vessels of pregnancy usually will permit placement of a 14-gauge cannula in the cepalic or basilic vein of the forearm. The disappearance of these veins owing to increased sympathetic tone may be a sign of hypovolemia, but also of cold and fear. A successful insertion of a small cannula is preferable to several failed attempts with a large one. If the patient is severely hypovolemic, central venous cannulation via the internal jugular or subclavian route may be more successful than peripheral. Peripheral venous cutdown requires equipment and expertise rarely found in the obstetric suite; it should be considered a measure of last resort. At the time of venous cannulation, a blood sample should be drawn, sufficient for analysis of hemoglobin/hematocrit, venous blood gases (a base deficit more than 4 to 6 mEq per L is abnormal, even in pregnancy), and blood type and antibody screen.

Infusion of Ringer's lactate or other balanced salt solution is begun; the first liter should be infused as rapidly as possible, while assessment of the patient proceeds. An estimate of the degree of hypovolemia must be made. Signs of impaired perfusion may be subtle, and estimates of external blood loss are inaccurate. Hypotension, tachycardia, pallor, clammy extremities, and other classic physical signs may or may not be present, depending on pain, anxiety, the degree of physiologic compensation, analgesic drugs administered during labor, and the rapidity of the blood loss. Hypotension is a late sign in the previously healthy young patient with ongoing hemorrhage. Therefore, measurement of serial blood pressures during a controlled physiologic challenge, such as placing the patient in a head-up position (tilt test) or infusing a liter of crystalloid, will indicate more about volume status than a single reading. A small dose of narcotic will produce exaggerated analgesic and vasodepressor effects in the hypovolemic patient; this can be a valuable test, but it must be administered cautiously.

ANESTHETIC MANAGEMENT OF POSTPARTUM COMPLICATIONS

The anesthesiologist must work concurrently toward assessing and preparing the patient for anesthesia. An efficient preanesthetic history is taken as the monitors are applied, venous cannulation is performed, and the physical examination is done (never neglecting, despite the urgency of the situation, a careful evaluation of the airway). Volume resuscitation is begun, and appropriate help is summoned. The plan for obstetric intervention must be laid out in advance. It usually will proceed from examination, perhaps under anesthesia, in steps of increasing invasiveness as needed. Since the anesthetic approach is tailored to the obstetric intervention, a number of conditions will be described, both to explain the obstetrician's goals and procedures and to describe the appropriate anesthetic response.

Uterine Inversion

Obstetric Considerations. Uterine inversion, although rare, is considered first because it may require immediate induction of general anesthesia if it is to be successfully treated.[7, 8, 13] The clinical setting is that of a poorly contractile, often multiparous uterus inverted as the result of traction on the umbilical cord of a fundally implanted placenta, which has not yet separated. A portion or all of the inner surface of the uterus appears at the cervix, while the fundus is not palpable abdominally. Brisk hemorrhage ensues. Shock presents quickly, perhaps "out of proportion to the blood loss" because of vagal stimulation, but more often in proportion to the blood loss, which is easily underestimated. Immediate volume resuscitation must be begun. Attempts to separate the placenta before reduction increase blood loss. The fundus must be reduced quickly, because hemostasis is impossible in the inverted position and because contraction of the lower uterine segment progressively entraps the fundus. If immediate reduction is impossible, the obstetrician will request uterine relaxation with a volatile anesthetic.

Anesthetic Considerations. Rapid sequence intravenous induction of general anesthesia under cricoid pressure, utilizing succinylcholine and a reduced dose of ketamine or thiopental is required as soon as it may safely be accomplished. Of course, adequate basic monitoring, venous access, and examination of the patient are necessary prerequisites. The most common volatile agent used is halothane administered through the endotracheal tube in order to relax the lower uterine segment and permit reduction by steady pressure on the fundus from below. Although "deep halothane" anesthesia is the usual request, an already hypovolemic patient may be very sensitive to the cardiopressant effect of halothane; therefore, an initial attempt at uterine reduction prior to initiating the volatile agent should be encouraged. Often the uterus may be replaced without the addition of halothane or other volatile agents. If reduction is not quickly accomplished, the addition of 1 to 2.5% halothane is warranted according to patient tolerance and obstetric success. Once the fundus has been reduced, sustained uterine contraction is necessary to maintain the reduction. The halothane is turned off, and pulmonary excretion is enhanced by mild hyperventilation. Oxytocin is added to the intravenous infusion (20 to 40 U per L) and intramuscular ergonovine, methyl ergonovine, or 15-methyl prostaglandin F_2 alpha may be required to achieve satisfactory uterine tone. A neuromuscular blocking drug and perhaps a narcotic are added to facilitate tolerance of the endotracheal tube while volume resuscitation is effected. Once the patient is clinically stable, mechanical ventilation is discontinued and the patient is extubated. Enflurane and isoflurane are probably equally useful as uterine relaxants in this circumstance, but extensive clinical experience is lacking; isoflurane may have some advantage in producing rapidly reversible uterine relaxation because it is the least soluble of the three.

Lacerations of the Birth Canal

Obstetric Considerations. The most common obstetric intervention, routinely undertaken following every delivery, is a through examination of the perineum, vagina, and cervix. This is followed by repair of any significant lacerations or tears, usually under local infiltration anesthesia with verbal reassurance as needed. However, if the laceration is extensive, or if the patient or the obstetrician displays unusual anxiety, intervention by the anesthesiologist may be appropriate.

Anesthetic Considerations. If visualization and repair of minor lacerations of the birth canal are the only interventions necessary, the hazards and inconvenience of initiating either general anesthesia or major regional block argue against their routine use. Repair of extensive lacerations of the cervix or perineum and drainage of paravaginal hematoma, in which the exquisite discomfort may prevent examination or even positioning for repair, are often best accomplished with low spinal anesthesia (T_{10} to S_5). General anesthesia may be indicated for the rare patient whose loss of self-control creates a danger for herself or others.

A well-functioning epidural catheter previously placed for labor analgesia may be reinjected if analgesia is insufficient for examination and repair. Reinjection may extend the sympathectomy; additional intravenous fluid may be required if blood loss has been significant.

Conscious sedation is also appropriate for many patients. As with general anesthesia, the drugs administered should be matched to the specific needs of the individual patient. The patient who reacts to the stress of the situation by overt expression of anxiety, or by exaggerated withdrawal responses to trivial stimuli, will benefit from the administration of sedative-hypnotic drugs. These include thiopental in small doses (1 mg per kg) ketamine (0.2 to 0.4 mg per kg), or midazolam (1 to 2 mg), repeated as necessary. Droperidol should only be added to these agents with great caution, if at all, because of its potential for enhancing the patient's fear even while diminishing her expression of it. If the patient's primary problem is an appropriate response to painful stimuli, the administration of analgesic drugs is indicated. Fentanyl, titrated to comfort in 0.5 to 1.0 μg per kg boluses, is well suited to this purpose because of its rapid onset, relatively brief duration of action, and absence of adverse cardiovascular effects.

Uterine Exploration and Curettage

Obstetric Considerations. If inspection of the birth canal does not reveal an extrauterine source of bleeding, the obstetrician's next step is bimanual examination of the uterus and exploration of the uterine cavity. Retained products of conception are detected and removed by systematic exploration of the endometrium, either by a large blunt ("banjo") curet or by a gauze sponge wrapped around the obstetrician's gloved second and third digits ("gauze curettage"). The uterine cavity is sounded, adherent placenta or fetal membranes are sheared away, and the uterus is emptied of blood, clot, and placental residua. The evacuated uterus is stimulated by bimanual massage and oxytocin infusion to produce mechanical hemostasis. Continued deep palpation and massage may be necessary over the ensuing hours to ensure that the fundus remains tonically contracted.

Anesthetic Considerations. Uterine curettage is usually accomplished in 5 minutes or less, so that it represents a very brief but intense stimulus. It may sometimes be successfully performed immediately after delivery without anesthesia (although not without discomfort). The anesthesiologist may be consulted after this has been unsuccessfully attempted. The ideal anesthetic technique would allow rapid induction, adequate analgesia, and swift recovery, while exposing the patient to no additional risks. In practice, clinical judgement is required to balance the goals of perfect analgesia, amnesia for the operation but not for the whole birthing experience, and avoiding the risks of aspiration and sympathectomy-induced hypotension. The anesthetic options are similar to those employed for lacerations of the birth canal.

If an epidural block was used for labor and delivery, provision of a level extending from T_{10} to S_5 will allow uterine exploration and curettage. The patient may be aware of vaginal pressure, and she should be so forewarned, but this is seldom troublesome. If the block has worn off, reinjection of the catheter with 10 mL of 1.5 to 2% lidocaine or 3% chloroprocaine in a semi-sitting position will rapidly re-establish analgesia; an additional liter of intravenous Ringer's lactate will prevent hypotension in the normovolemic patient. Hypotension despite this volume preload indicates that the patient's blood volume deficit has been underestimated. The addition of 3 to 4 mg of preservative-free morphine or 100 μg fentanyl to the epidural space is very useful to provide prolonged post-procedural analgesia to permit ongoing uterine palpation and massage.

Spinal anesthesia may rapidly be induced for uterine curettage. The rapid onset of sympathectomy may also unmask unsuspected hypovolemia, particularly if the block extends above T_{10}; prophylactic volume loading and prompt treatment of hypotension are indicated. A small dose of hyperbaric lidocaine (30 to 60 mg), procaine (50 to 100 mg), or bupivacaine (6 to 7.5 mg) with appropriate positioning will provide a modified saddle block, extending from T_{10} to S_5. Although the short latency and duration of procaine are ideally suited to this procedure, the drug is seldom used in modern practice. The choice of spinal anesthesia does expose the parturient to the risk of post–lumbar-puncture headache, which is an important consideration for such a short procedure.

Even if the uterus has been stimulated to contract, the postpartum cervix will usually admit the obstetrician's fingers or curet if adequate analgesia is provided. Rarely, general anesthesia with uterine relaxation is required. In this rare case, rapid sequence induction and endotracheal intubation are indicated to protect the unconscious patient's airway. Halothane is cautiously administered via the endotracheal tube. Other agents have been used for uterine relaxation, including inhaled amyl nitrite and intravenous terbutaline and nitroglycerin. There would seem to be little advantage to these over the use of an inhaled vapor familiar in its effects to every anesthesiologist. Halothane, or its alternatives, enflurane and isoflurane, has the advantage of titratability, reliability, and predictability.

Conscious sedation may be used to provide swift induction of analgesia and amnesia without unconsciousness and its attendant hazards. In the patient with an uncertain volume status, it provides minimal physiologic disturbance. Midazolam, 1 to 2 mg intravenously, provides a baseline of sedation and amnesia. Alternatives are ketamine, in 0.2 mg per kg increments or alfentanil in 5 to 10 μg per kg increments. Two or more of these may be added together with extreme caution because it is easy to cross the boundary between conscious sedation and general anesthesia with an unprotected airway. Supplemental oxygen is required with these adjuncts, because they produce transient respiratory depression. Nitrous oxide 20 to 60% may be added for additional analgesia and sedation, but it must be carefully titrated to maintain patient response to verbal stimuli.

Ketamine is the mainstay of conscious sedation, because a small dose will reliably and briefly provide analgesia and amnesia without significant depression of protective airway reflexes or of respiratory or cardiovascular function. However, it must be appreciated that the onset is not immediate (1 to 3 minutes) and that purposeless vocalization and movement in response to stimulation is common. It is better to accept these untidy responses, as long as operating conditions are adequate, than to progressively increase the dose in pursuit of immobility. Higher doses prolong recovery and increase the incidence of disturbing hallucinations. Midazolam premedication and verbal reassurance, including answering the characteristic repetitive questions, smooth the emergence from ketamine analgesia. A theoretical concern has been raised[11] that ketamine may raise uterine tone and thereby make introduction of the curet difficult. This problem is rarely, if ever, realized in practice as this effect is dose dependent and insignificant at doses of less than 2 mg per kg.

Atony and Persistent Bleeding

Obstetric Considerations. Atony is a diagnosis of exclusion, justifiable only when the uterus is known to be empty and extrauterine sources of bleeding have been ruled out. Hormonal stimulation with oxytocin, 40 to 200 mU per minute, is adequate to produce tetanic contraction in the normal uterus. This is commonly administered by adding 20 U per L to the patient's intravenous fluid immediately following delivery.

In the patient with persistent atony, replacement of blood volume may require rapid intravenous fluid administration. If that fluid contains 20 U per L oxytocin, then at high infusion rates one may produce a profound vasodilator effect due to the high dose of oxytocin. Under this circumstance, hypotension may worsen rather than improve.

Therefore, in this circumstance, either the oxytocin infusion should be "piggy-backed" into the volume line, or the concentration of oxytocin should be reduced to 5 U per L in each container of intravenous solution to be rapidly infused.

Atony may persist despite oxytocin administration, particularly in the situations of prolonged labor, stimulated labor, uterine overdistension, grand multiparity, and sepsis. Recently, 15-methyl prostaglandin F_2 alpha (Prostin15M) has proved to be a valuable agent to stimulate the refractory myometrium.[1, 6, 12] Although it may be administered intramuscularly in a dose of 250 μg, intramyometrial administration is popular. Nausea is a common side effect, but bronchoconstriction and systemic or pulmonary vasoconstriction are possible, and significant arterial desaturation has been reported, albeit transient.[5]

Ergonovine or methylergonovine, 0.2 mg intramuscular, stimulate smooth muscle contraction generally, including myometrium. Catastrophic hypertension is possible if either is administered in the presence of pre-existent hypertension or large doses of vasopressors, or if this dose is given as an intravenous bolus. Although the ergot derivatives are still given by tradition, the uterine-stimulating effect of the more modern prostaglandin seems to be more specific and efficacious. These pharmacologic therapies may be augmented by uterine massage. Bimanual compression of the uterine arteries may also decrease the rate of bleeding while volume resuscitation catches up to the blood loss. Packing the uterus with warm saline gauze is a technique mentioned in textbooks of obstetrics but seldom if ever practiced today.

If bleeding persists after prostaglandin stimulation, refractory atony, abnormal placentation, or a tear in the corpus uteri is likely to be responsible. Surgical management is the next obstetric step, except in centers where radiographically guided selective arterial embolization may be carried out. If the patient desires to remain fertile, the goal of operation is to interrupt the major blood supply to the uterus, preserving uterine viability by means of the myriad pelvic anastomoses but reducing the perfusion pressure enough to produce stasis, platelet aggregation, and clotting at the bleeding sites. This may be accomplished by embolization or surgical ligation of the uterine or hypogastric arteries. Uterine artery ligation is easily performed but less often successful; hypogastric artery ligation is difficult surgery in a gravid pelvis, and it usually entails considerable additional blood loss. If fertility is not a high priority, or if the patient is already in extremis, hysterectomy is the most expeditious way to achieve hemostasis. Supracervical hysterectomy is the easier procedure in the highly vascular gravid pelvis, but total hysterectomy may be necessary if the placental implantation is low. Placenta percreta, an exceedingly rare condition in which the trophoblast has invaded adjacent pelvic structures, may require unusual measures.

Anesthetic Considerations. If persistent atony or abnormal placentation is present at cesarean section, the diagnosis is obvious, and definitive surgery may be carried out without delay. On the other hand, after vaginal delivery, the decision to operate is often delayed until the patient is severely hypovolemic. If the anesthesiologist is consulted early, appropriate monitoring and volume resuscitation may be instituted, so that the decision to operate may be based on the intractability of the bleeding rather than on a previously healthy patient's deteriorating condition. If the patient is volume replete at the time of induction, regional anesthesia has a limited role in this situation, although its successful use has been reported.[2] Impaired ventilation, inadequate analgesia, and patient discomfort during regional block may distract the anesthesiologist from essential resuscitative tasks.

A general anesthetic technique should be tailored to rapidly control the airway and allow resuscitation. Additional venous access should be secured prior to induction, if necessary, by a central route. Central venous and systemic arterial pressure monitoring may be exceedingly valuable, but these should not delay definitive therapy. Succinylcholine and ketamine (0.5 to 1 mg per kg) may be supplemented at induction with fentanyl analgesia, with muscle relaxation maintained by pancuronium or vecuronium. The volatile anesthetics are best avoided initially because they may aggravate uterine atony even in low concentrations; amnesia is attainable in the parturient with 60% nitrous oxide supplemented by narcotic, and the unstable patient may not even tolerate nitrous oxide. More important than the particular choice of drugs for anesthesia is ongoing communication with the operating surgeon and proper fluid resuscitation.

Transfusion will probably be necessary, certainly so if the surgeon makes heroic attempts to preserve fertility. If massive transfusion is necessary, several secondary complications may occur. Dilutional coagulopathy may become evident as the volume transfused exceeds one blood volume. Citrate intoxication may result from binding of ionized calcium during rapid transfusion, particularly if fresh frozen plasma plus packed cells are provided as a substitute for whole blood. Although this is usually a transient phenomenon, it may lead to impaired contractility in both myocardium and myometrium. Hypothermia and its associated complications may occur if rapidly infused blood and blood products are not warmed. Invasive hemodynamic monitoring, that is, central venous line or pulmonary artery catheter and arterial catheter, is most useful in the context of massive transfusion. When hemostasis is finally achieved, it often occurs abruptly; continued rapid transfusion may easily lead from hypovolemia to fluid overlead and pulmonary edema. If a prolonged period of hypoperfusion and shock has preceded surgical control of bleeding, multiple organ injury may occur, including damage to lungs (adult respiratory distress syndrome), kidneys (acute tubular necrosis), the immune system (sepsis), or, peculiar to pregnant women, posterior pituitary (Sheehan's syndrome). The intraoperative and postoperative prevention and management of these complications requires not only monitoring but also a comprehensive approach to the care of the patient. Postoperative care may better be carried out in an intensive care unit than in the obstetric suite.

Near the end of operation, the anesthesiologist and obstetrician must consider what physiologic monitoring and support will be required in the postoperative period. Even if postpartum hemorrhage has been promptly and appropriately treated, it represents a significant physiologic stress to the parturient; the full effects of this stress may not be immediately apparent. At a minimum, nursing care in the postoperative period should include recording of vital signs at frequent intervals until stable, hourly urine output; serial determinations of hemoglobin, hematocrit, electrolytes, and arterial oxygen saturation; and a low patient-to-nurse staffing ratio. If the patient is not yet physiologically stable at the end of operation, the anesthesiologist must decide whether to continue ventilatory support and invasive hemodynamic monitoring in the operating room, intensive care unit, or obstetric suite depending on the nursing capabilities available.

Selective Arterial Embolization

Obstetric Considerations. In institutions where there are angiographers with the requisite skill and experience, selective pelvic artery embolization may be considered a first-line and preferable treatment for refractory hemorrhage, particularly when preservation of fertility is a high priority.[3, 4] Embolization may allow a more selective obliteration of the bleeding source while preserving the viability of the uterus and adjacent pelvic structures. A surgical operation is avoided, and damage to the ureters, bladder, and rectum is less likely.

Initial evaluation and resuscitation is appropriately carried out in the operating room. If hemorrhage persists despite nonsurgical measures and the patient is stable, medical consultation with the angiographer is arranged. The patient is transferred to the angiography suite, and diagnostic angiography is performed. The primary feeding artery is selectively cannulated, and thrombogenic material is injected to embolize to the bleeding site. Surgical gelatin sponge, autologous blood clot, and a variety of mechanical devices have been used to create occlusion.

Anesthetic Considerations. Femoral artery catheterization may be carried out under local anesthesia; however, conscious sedation may make the procedure less unpleasant for all concerned. Midazolam, 1 to 2 mg, is usually sufficient, and this may be given routinely by the angiographer. However, the patient with postpartum hemorrhage may require the care of an anesthesiologist in the angiography suite for hemodynamic monitoring and resuscitation. Diagnostic angiography and selective cannulation may require considerable time, during which the hemorrhage continues. Adequate renal blood flow and diuresis must be maintained to avoid the nephrotoxic effects of the radiographic contrast medium.

Maintaining adequate delivery of blood products in a location outside the operating area may require additional support personnel beyond those who staff the angiography suite. Invasive hemodynamic monitoring in such an unusual location may also require advance planning.

SUMMARY

Postpartum hemorrhage results from trauma to the birth canal, or from a failure of the mechanical occlusion of the spiral arterioles normally effected by the contracting myometrium. The anesthesiologist must be prepared to provide massive transfusion if necessary, as well as analgesia and anesthesia for examination of the birth canal, exploration and curettage of the uterus, surgical or angiographic occlusion of the hypogastric arteries, or hysterectomy. Communication between anesthesiologist and obstetrician is essential; depending on the obstetric intervention, uterine relaxation by anesthetic vapors may be absolutely necessary or contraindicated.

REFERENCES

1. Buttino L, Garite TJ: The use of 15 methyl-F_2-alpha prostaglandin (Prostin15M) for the control of postpartum hemorrhage. Am J Perinatol 3:241–243, 1986
2. Chestnut DH, Dewan DM, Redick LF, et al: Anesthetic management for obstetric hysterectomy: A multi-institutional study. Anesthesiology 70:607–610, 1989
3. Glickman MG: Pelvic artery embolization. *In* Berkowitz RL (ed): Critical Care of the Obstetric Patient. New York, Churchill Livingstone, 1983, pp 165–187
4. Greenwood LH, Glickman MG, Schwartz PE, et al: Obstetric and nonmalignant gynecological bleeding: Treatment with angiographic embolization. Radiology 164:155–159, 1987
5. Hankins GD, Berryman GK, Scott RT Jr., et al: Maternal arterial desaturation with 15-methyl prostaglandin F_2-alpha for uterine atony. Obstet Gynecol 72:367–370, 1988
6. Hyashi RH, Castillo MS, Noah ML: Management of severe postpartum hemorrhage with a prostaglandin F_2-alpha analogue. Obstet Gynecol 63:806–808, 1984
7. Kitchin JD III: Puerperal inversion of the uterus. Am J Obstet Gynecol 123:51–58, 1975
8. Platt LD, Druzin ML: Acute puerperal inversion of the uterus. Am J Obstet Gynecol 141:187–190, 1981
9. Rochat RW, Koonin LM, Atrash, et al: Maternal mortality in the United States: Report from the Maternal Mortality Collaborative. Obstet Gynecol 72:91–97, 1988
10. Sachs BP, Brown DA, Driscoll SG, et al: Maternal mortality in Massachussets. Trends and prevention. N Engl J Med 316:667–672, 1987
11. Shnider SM, Levinson G: Anesthesia for Obstetrics, ed 2. Baltimore, Williams & Wilkins, 1987, p 288
12. Toppozada M, El-Bossaty M, El-Rahman HA: Control of intractable atonic postpartum hemorrhage by 15-methyl prostaglandin F_2 alpha. Obstet Gynecol 58:327–330, 1981
13. Watson P, Besch N, Bowes WA Jr.: Management of acute and subacute puerperal inversion of the uterus. Obstet Gynecol 55:12–16, 1980

Address reprint requests to

Walter L. Millar, MD
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Postcesarean Section Pain Prevention and Relief

*Joanna Brown Sullivan, MD**

Unlike most surgical patients, many parturients express the desire to be awake and alert during and after childbirth. This healthy group of patients usually requests the minimum amount of medication during labor, delivery, and during the postoperative period, seeking to avoid maternal and infant side effects. The recovery should be compatible with the initial newborn bonding and frequent feeding. Comfort is important to enable meaningful interaction with family members since there is often a steady stream of well wishers after the delivery. With traditional postcesarean section pain management, the goals of comfort without sedation and avoidance of maternal and neonatal adverse effects are frequently not attained.

Postoperative analgesia is currently the most dynamic and investigated topic in obstetric anesthesia. Women experiencing the pain of childbirth are among the primary benefactors of recent discoveries and clinical contributions. Responding to vocal patient preferences, new comfortable obstetric units boast home-like settings and offer 24-hour-a-day anesthesia care. The role of the obstetric anesthesiologist has been enhanced to include providing safe and satisfying postoperative pain relief to the parturient. Among newer choices for providing analgesia are intraspinal opiates during labor, surgical delivery, and the postoperative period. In addition, patient-controlled analgesia (PCA) devices deliver bedside, individualized doses of postoperative pain relief. These new techniques are not without side effects and risks.

ORIGIN OF OBSTETRIC PAIN

Peripheral Pain Pathways

The activation of sensory structures that detect ongoing tissue injury and transmit pain information to the cortex is termed nocicep-

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*Assistant Professor of Clinical Anesthesia, University of California, San Francisco, San Francisco, California

tion. The injury-sensitive nerve endings are called nociceptors. These receptors are activated by any noxious mechanical, thermal, or chemical stimulus. Nociceptors are organ dependent as to the type of mechanical stimulation that is transmitted, with a range of frequency response and duration that is relatively specific for the type of pain. Surgical incision of the skin will be acknowledged by the pain receptors. Stretching of the skin will not be perceived as pain in contrast to the marked activation of nociceptors with distention of abdominal and pelvic viscera. The portion of the sensory afferent nerve fibers that transmit injury impulses are the A-delta and the C fibers. The rapid transmission of pain signals involves the A-delta fibers. These thinly myelinated sensory afferent fibers require a very strong stimulus, one that is clearly damaging to the tissue. This rapid injury current results in very specific localization of the injury origin. The slower-conducting unmyelinated C fibers is the constant, aching quality of pain, poorly localized to the source.

The afferent nerve fibers from the uterus and cervix are somatic sensory fibers that travel with the sympathetic nervous supply of the uterus and enter the spinal cord through the 10th, 11th, and 12th thoracic nerves. These fibers transmit the pain of the first stage of labor, the contractions of the uterus, and dilation of the cervix. These afferent fibers pass through the paracervical tissue along the uterine artery and then through the inferior, middle, and superior hypogastric plexuses to the sympathetic chain. Impulses arriving from the vagina, vulva, and perineum initiated during the second stage of labor travel a different pathway. Sensory innervation during vaginal delivery is transmitted through the pudendal nerve, which enters the CNS via the second, third, and fourth sacral nerves. Following cesarean section, the lower abdominal skin incisional area sends cutaneous pain impulses along the lower lumbar sensory afferent fibers to the spinal cord.

Central Pain Pathways

Upon entering the CNS, these nociceptive impulses undergo a modulation process in the posterior horn of the spinal cord. The main nociceptive input to the dorsal horn of the spinal cord is of cutaneous origin. Approximately 10% is visceral. Here in the substantia gelatinosa (laminae I and II) there is a high density of staining for mu-sites, kappa-sites, and delta-sites. Thus, the staining pattern coincides with the termination areas of the C fibers, which supports a role for opioids in "gating" nociception at the spinal cord level.[33] Wide dynamic response neurons found in the dorsal horn with the neurotransmitters released in the substantia gelatinosa modify nociception by information from descending inhibitory pathways or excitatory crosstalk amplification.

After passing through the dorsal horn, the injury signal travels upward from laminae I, II, V, and VI, primarily through the neospinothalamic and paleospinothalamic tracts to the reticular formation in the brainstem. Pain perception in the reticular formation is capable of eliciting a systemic catecholinergic pain response, complete with tachycardia, increased blood pressure, and hyperventilation. From the brain stem, the multisynaptic ascending pathways pass to the posterolateral nucleus of the thalamus, then to the cortex, and results in the perception of postoperative pain.

OPIATES AS ANALGESICS

Extracted from the poppy, the opium alkaloid was named morphine after the Greek goddess of sleep, Morphina (or the Greek god of dreams, Morpheus), in 1803 by Fredrich Meisner.[36] Through the years, other compounds possessing the phenanthrene ring as a base structure were introduced for clinical use in the United States: hydromorphone, 1926; meperidine, 1938; fentanyl, 1968; sufentanil, 1984; and alfentanil, 1987. These compounds all yield a dose-dependent blunting of the response to painful stimulation, respiratory depression, and intestinal transit delay. These opioid drugs act on stereospecific and saturable receptors in the CNS and other tissues: central periaquaductal grey and spinal cord dorsal column substantia gelatinosa producing analgesia; solitary nucleus resulting in depression of cough reflex; chemoreceptor trigger zone eliciting nausea and vomiting; medullary respiratory center causing respiratory depression; peripheral and central neurogenic promoting urinary retention; and peripheral smooth muscle contributing to delayed intestinal transit.

Opiates have been the mainstay of postoperative pain management, traditionally administered intramuscularly on an as-needed basis. After absorption, blood concentrations of opiate must be above the minimum effective analgesic concentration to achieve pain relief. Unfortunately, there is no effective way of estimating the individual daily analgesic need. Due to a large amount of interpatient variability in the minimum effective analgesic concentration and a relatively small difference in concentration resulting in adequate analgesia versus moderate pain, many patients experience postoperative pain.[15, 16]

In 1988, two separate meritorious studies[19, 24] compared various analgesic strategies for postcesarean pain relief. The control groups in both studies received the conventional as-needed intramuscular morphine or meperidine, typical of most postoperative pain management plans. In each study, patients were randomly assigned to one group (intramuscular versus PCA versus intraspinal morphine), and pain assessments were made for 24 hours following cesarean section. In Harrison's study,[24] 94% of the patients receiving conventional intramuscular analgesia reported moderate to severe pain throughout the observation period. In Eisenach's study,[19] feelings of pain or discomfort were reported significantly more frequently in the group receiving traditional intramuscular opiates. Clearly, the routine administration of intramuscular opiates does not provide satisfactory analgesia following surgical delivery.

Table 1. *Probable Subclassification of Opioid Receptors and Respective Agonists/Antagonists*

RECEPTOR	AGONIST	ANTAGONIST
mu Analgesia, miosis, respiratory depression	Morphine, fentanyl sufentanil, alfentanil methadone, hydromorphone, meperidine, DAGO, buprenorphine	Naloxone, B-FNA
delta Analgesia?	DPDPE, DSLET	Naloxone
kappa Sedation, analgesia, no respiratory depression	Butorphanol, nalbuphine, binaltorphimine, bremazocine, spiradoline	Naloxone
epsilon	B-endorphin	Naloxone
sigma Excitatory symptoms: hypertonia, tachycardia, tachypnea	PCP SKF-10047	—

Abbreviations: DAGO, D-Ala2-MePhe-Glyol-enkephalin; DPDPE, D-Pen2-D-Pen5-enkephalin; DSLET, D-Ser2-Leu5-enkephalin-Thr6; PCP, phencyclidine; SKF-10047, N-allylnorcyclazocine.

Adapted from Yaksh TL, Al-Rodhan NRF, Jensen TS: Sites of action of opiates in production of analgesia. *In* Fields HL (ed): Progress in Brain Research. New York, Elsevier, 1988.

INTRASPINAL OPIATES

In 1975, the discovery of enkephalins by Hughes, and endorphins by Pert and Snyder, initiated the opioid receptor theory and study of pain mechanisms. In 1976 Yaksh and Rudy[55] reported the presence of these opioid receptors in the spinal cord and demonstrated that intrathecal administration of morphine produced dose-related pain relief in rats. This suggestion that intraspinal opiates could control pain was soon followed by the first clinical report of intrathecal opioids providing pain control in cancer patients.[51] Recently, the isolation of receptor subclasses and identification of their selective physiologic action has provided insight into the action of several drugs.[54] These distinct subclasses of opioid receptors have significant relevance to clinical utilization (Table 1).

Within a relatively short time, the technique of injecting opioid drugs into the epidural and intrathecal space has become well established in the management of acute postoperative pain, including postcesarean section pain. Since its introduction in 1979, this analgesic technique has grown in popularity and acceptance. Within the last 10 years, spinally administered opiates have become part of the innovative armamentarium available to the anesthesiologist caring for the parturient. The use of intraspinal opiates continues to increase. In a 1988 survey by Knapp and Writer[27] of the Society for Obstetric Anesthesia (SOAP) members, 77% of those responding were using epidural opiates to treat postoperative pain. The most common solutions were either epidural morphine, 4 to 5 mg or fentanyl, 50 to 100 μg, or both, approximately 8:5 in favor of epidural morphine. Reports on optimal dose, prevention and treatment of side effects, safe monitoring of risks, and acknowledged limitations of this technique appear monthly in anesthesiology and obstetric journals. Clearly, women experiencing childbirth are the benefactors of this abundant interest and research activity.

Opiates injected into either the epidural or intrathecal space provide pain relief after cesarean section and lower-extremity, abdominal, and thoracic surgery.[4, 13, 42, 45, 49] Analgesia produced by epidural and intrathecal administration of opioids is different from and superior to analgesia achieved by the routine as-needed administration of narcotics.[11, 19, 24, 30, 47] Epidural morphine provides superior analgesia with clinically inconsequential increase in side effects when compared with patient-controlled intravenous morphine.[30] This superior antinociception effect can be achieved without affecting motor, sympathetic or proprioceptive pathways. The benefits of intraspinal opiate administration after various surgeries are well documented. For the woman experiencing surgical childbirth, the combination of intrathecal morphine and local anesthesia provide both excellent intraoperative anesthesia and postoperative analgesia. Similarly, epidural opiates administered after the delivery provide long-lasting and satisfactory analgesia after cesarean section.

Intraspinal Opiates for Control of Postcesarean Section Pain

Intraspinal opiates have emerged as the "gold standard" for providing optimal postoperative analgesia. Efficacy and safety have been shown for use of epidural morphine for post-surgical pain management after peripheral vascular and orthopedic procedures in well-done dose-response studies.[4] In addition, epidural and intrathecal placement of opioids is highly effective in alleviating pain following cesarean section, with an acceptable incidence of side effects. The pain relief provided by intraspinal opiates is exceptionally better than traditional intramuscular morphine administered as needed,[19, 24, 30] and significantly better than PCA.[19, 24] Obstetric patients receiving intraspinal opiates require fewer supplemental opiates.[45, 48] They voice greater satisfaction with epidural and intrathecal analgesia when compared with routine intramuscular pain control.[19, 24]

In this group of young and generally healthy patients with infrequent morbidity and mortality, efforts to improve patient outcome are difficult to evaluate. Earlier sitting, standing, and ambulation occur in patients receiving intraspinal analgesia.[10, 41] There is earlier return of bowel function,[41] with shorter interval from operative delivery to tolerating sips of water. There may be a decreased incidence of post-spinal headaches in patients receiving intrathecal morphine.[40] A group from the University of Washington[48] reported significantly shorter hospital stays for the cesarean section patients given intrathecal morphine. Even in the low-risk cesarean population, there may be a more rapid recovery or decreased morbidity resulting in shorter hospital stays and reduced financial expenditure for the patients. In several ways, comfort and satisfaction with the birthing experience can be improved with intraspinal opiates. Ackerman et al[3] report decreased nausea and vomiting during uterine eventration. Nausea or emesis or both can occur in awake patients undergoing cesarean section during uterine manipulation and eventration despite adequate sensory levels and normal blood pressures. Epidural fentanyl administered immediately after delivery has been shown to decrease this noxious response. The reason is unknown, but may be related to potentiation of bupivacaine by the epidural opioids.[3] Following completion of the surgical delivery, epidural and intrathecal opiates do not interfere with initiation and completion of maternal-infant bonding.[10]

Regional anesthesia combined with intraspinal opiates for postoperative analgesia has been shown to decrease morbidity in high-risk surgical patients.[41, 47, 56] Intraspinal opiates during labor and delivery have been effective in some groups of high-risk obstetric patients, improving maternal and infant outcome. Epidural opiates help restore postoperative respiratory function, preserving the FVC and FEV1 when compared with intravenous analgesia following thoracic surgery.[47] Obese patients hospitalized for a gastric bypass operation had reduced incidence of pulmonary complications, earlier return of bowel function, earlier ambulation, less deep venous thrombosis, and shorter hospital stays.[41] These desired results can also be achieved with intermittent injections of intrathecal opiates or continuous infusions of epidural morphine.[13, 29, 43]

Epidural Opiates for Postcesarean Analgesia

The optimal dose of preservative-free morphine for providing safe and effective analgesia following cesarean section appears to be in the 4- to 5-mg range. Most patients will receive 16 hours[10] to 24 hours[45] of satisfactory analgesia, often receiving no additional opiate supplements. The transition to oral analgesic medication usually follows easily. Rosen et al[45] demonstrated that a 2-mg dose of epidural morphine was ineffective in controlling postcesarean section pain. On the other hand, doses of 7.5 mg and greater have not been found to provide better analgesia and have been associated with a higher incidence of bothersome side effects.

Morphine is probably the most common opiate administered to the epidural space to establish post-surgical delivery analgesia. Other opiates, with characteristic time to onset and duration of action, are also successful in providing analgesia. Fentanyl has been used both as a single dose and as a continuous infusion to attain postcesarean analgesia. It has been demonstrated that 50 μg of epidural fentanyl after cesarean section provides analgesia beginning in about 7 minutes and lasting approximately 5 hours.[32] Epidural fentanyl appears to have a somewhat lower incidence of bothersome pruritus when compared with epidural morphine.[32] Pruritus has been attributed to the cephalad

Table 2. *Molecular Weight, pKa, and Lipid Solubility for Various Opiates*

OPIATE	MOLECULAR WEIGHT	pKa	OCTANOL-WATER PARTITION COEFFICIENT*
Morphine	285	7.9	1.4
Meperidine	247	8.5	39
Alfentanil	417	6.5	89
Methadone	309	9.3	116
Fentanyl	336	8.4	816
Sufentanil	386	8.0	1727

* *Adapted from* Hug Jr CC: Pharmacokinetics of new synthetic narcotic analgesics. *In* Estafanous FG (ed): Opioids in Anesthesia. Boston, Butterworth, 1984.

spread of hydrophilic morphine,[11] and occurs less frequently with the lipophilic opiates.

Sufentanil at doses ranging from 30 to 60 μg provides analgesia within 15 minutes following dosing, yet lasts only 4 to 5.5 hours, respectively.[44] This short duration of action of relatively large doses of sufentanil may be due to rapid uptake of this agent by adjacent tissues, particularly the surrounding vasculature. Despite the higher lipid solubility, Rosen and his group[44] did not find a lower incidence of side effects when compared with epidural morphine 5.0 mg, with the exception of pruritus, which had 17% incidence with epidural sufentanil versus 50% with epidural morphine.

Epidural hydromorphone may be preferable to other opiates, excluding morphine, in providing effective analgesia after cesarean delivery because it has a longer duration of action than epidural methadone, meperidine, fentanyl, and sufentanil. Hydromorphone (Dilaudid) 1.0 mg and 1.5 mg given in the epidural space provided between 13 to 19 hours of postcesarean analgesia[9, 25, 46] and epidural hydromorphone with epinephrine hastened the onset of postcesarean analgesia and increased the duration of analgesia to 24 hours.[18] In addition, the readily available commercial preparation Dilaudid is preservative-free, eliminating the need for a specially formulated preparation for epidural use. Meperidine is another opiate that is safe and effective when used as epidural analgesia. Epidural meperidine 50 mg produces better pain relief than epidural placebo or intramuscular meperidine 100 mg, yet has the same duration of action as the intramuscular injection, lasting 2.5 to 3.0 hours.[5] The physicochemical characteristics of these drugs are summarized in Table 2.

Single-dose administration of epidural or intrathecal analgesia is frequently adequate in mitigating the postoperative pain of a cesarean section. For pain control incurred after various other surgeries, studies have reported the success and safety of intermittent and repeated doses of epidural opiate analgesics.[42, 43] In addition, continuous epidural opioid infusions have been used with greater convenience and apparent similar safety after many operations.[29, 47] The caudal route is a successful alternative to the usual choice of lumbar epidural placement. In patients with a reason to avoid lumbar placement of epidural catheter, caudal administration with manipulation of the opiate dose and volume will result in good postoperative analgesia. Patients with a previous laminectomy, thoracolumbar rodding procedure, severe scoliosis, or a lumbar cutaneous lesion may present a problem for a successful placement of a lumbar epidural catheter. Total pain relief can be attained for post-thoracotomy pain by administration of morphine through a catheter placed in the caudal epidural space. A somewhat higher dose (10 mg) diluted to a higher volume (diluted in 10 to 20 mL of preservative-free normal saline) is needed to provide satisfactory pain control.[5]

Intrathecal Opiates for Postcesarean Pain Relief

The intrathecal route of administration of morphine circumvents diffusion barriers encountered with epidural dosing, hence a considerably lower dose is required to produce the same degree of analgesia. The effective and safe dose is much lower than initially used. Early studies of intraspinal narcotic administration suggested that the risk of delayed respiratory depression was greater after intrathecal morphine than after epidural morphine administration. These studies were conducted with intrathecal morphine doses ranging from 0.5 to 20 mg. Consequently, many obstetric anesthesiologists have been reluctant to give intrathecal morphine combined with local anesthesia at the time of cesarean section. Yet more recent data suggest that the dosages of intrathecal morphine given in earlier studies may have represented a relative overdose and that this route of administration for providing obstetric analgesia is viable.

Intrathecal administration of small doses of morphine provides excellent analgesia after cesarean section with minor side effects and with no depressant effects on ventilatory responses to CO_2. In a recent study by Abboud et al,[1] both doses of 0.1 and 0.25 mg resulted in excellent postoperative analgesia with long duration (18.6 ± 0.9 and 27.7 ± 4.0 hours, respectively) without significant side effects. Pruritus was mild and did not require treatment. Ventilatory responses to CO_2 showed no evidence of depression attributable to either the 0.25 or 0.1 mg intrathecal morphine. Significant depression of the CO_2 responses was observed in the placebo group patients after administration of 8.0 mg subcutaneous morphine. All neonates were vigorous at 5 minutes, and there was no significant difference between the incidence of low 1-minute Apgar scores among the three groups. Urinary retention was not evaluated as all patients required routine indwelling Foley catheters following cesarean section. Vomiting was significantly more common in the group receiving 0.25 mg intrathecal morphine than those receiving 0.1 mg (27 versus 0%). This incidence of vomiting is similar to a 12% rate of occurrence reported with 0.2 mg intrathecal morphine.[2]

In 1988, Chadwick and Ready[7] described how both intrathecal doses of 0.3 and 0.5 mg successfully ameliorated postcesarean pain.

They did add that doses greater than 0.3 mg may not be truly necessary for adequate analgesia. They postulated that there may be a ceiling effect for quality of analgesia in the approximate dose range of 0.25 to 0.3 mg, with minimal reduction in the duration of analgesia. The low end of efficacious intrathecal morphine dose is important in light of the fact that intrathecal opiates are associated with a higher incidence of respiratory depression than epidural morphine, though doses greater than 0.5 mg were used when ventilatory depression was observed. Hence, the recent reports of low-dose intrathecal morphine, 0.2 to 0.3 mg, usually combined with 0.75% bupivacaine anesthesia, document the satisfactory analgesia following cesarean section, complete with minimal side effects and no reported incidences of significant respiratory depression.

SIDE EFFECTS OF INTRASPINAL OPIATES

Cephalad spread of spinal opioids has been associated with the occurrence of side effects such as pruritus, nausea, and respiratory depression.[11] Morphine injected into the lumbar epidural area crosses several diffusion barriers and ascends in the subarachnoid space. Due to its hydrophilic nature, morphine penetrates into the cerebrospinal fluid (CSF) to such an extent that the concentrations in the lumbar CSF far exceed the corresponding plasma concentration. Within the lumbar CSF, morphine is transported to the fourth and lateral ventricles in a time-dependent fashion. Since the intrathecal route of administration deposits the morphine directly into the CSF, considerably lower doses are necessary to produce the same degree of analgesia. The CSF levels of morphine after intrathecal administration of 0.25 to 0.5 mg are still higher than those seen after epidural administration of a tenfold larger dose.[34]

Respiratory Depression

Respiratory depression after both intrathecal and epidural morphine may be immediate or delayed. Immediate depression from epidural dosing is caused by the rapid systemic absorption of morphine, with the concentration-time profiles closely resembling those obtained after intramuscular or intravenous dosing.[42] This early respiratory depression occurs within 10 to 15 minutes, corresponding to the time to peak plasma concentration, is easily diagnosed, and therefore is easily managed. The delayed respiratory depression that may not develop until 4 to 8 hours later proves to be a more serious condition, especially if monitoring of the patient is inadequate. In baboon studies, the maximal concentrations of tritium-labeled morphine were detected in the medulla oblongata 6 hours after injection in the lumbar area. This time corresponded to the occurrence of maximal ventilatory depression in these animals.[21] Delayed respiratory depression may be caused as a result of the affinity of morphine for binding sites, possibly opiate receptors, situated within the vital respiratory and cardiovascular neuronal complexes of the medulla.[21]

Estimates of the incidence of respiratory depression following epidural morphine have been placed at 0.09 to 0.4%.[23, 28, 38, 49] All agree that patients receiving intraspinal opiates should be monitored for 24 hours. Some advocate hourly observation and documentation of respiratory rate over a 24-hour period. Respiratory rate alone may not be sufficient to detect respiratory depression because it is known to be an unreliable indicator of depression in healthy volunteers. Others recommend documentation of hourly sedation evaluation and scoring, as ease of arousal may be a more accurate indicator of impending respiratory depression. The scoring of a sedation scale is presented: 1, wide awake; 2, drowsy; 3, sleeping; 4, difficult to arouse; and 5, does not awaken when aroused.

Epidural alfentanil and sufentanil can cause immediate respiratory depression similar to parenterally induced respiratory depression. This immediate effect on respiration is secondary to rapid systemic absorption of these lipophilic drugs, with results appearing similar to intravascular injection.[35] The potential delayed respiratory depression is due to the rostral spread of the drug.

Nausea

Systemic opioids administered by the intramuscular or intravenous route to treat postoperative pain can stimulate the chemoreceptor trigger zone (CTZ) of the medulla, producing nausea and vomiting. This central emetic effect is also the presumed mechanism of action of intraspinal opiates. Nausea is a commonly reported side effect with an incidence of 29% following low-dose intrathecal morphine[2] to 60% following epidural morphine.[11] Vomiting during the recovery period after a cesarean section is in the range of 12%[2] to 27%[1] following low-dose intrathecal morphine.

Movement and assuming an upright position boost the likelihood of nausea, suggesting a significant additional vestibular component to the central stimulation. Drugs that are useful in reducing motion sickness are helpful in reducing systemic opiate-induced emesis. Scopolamine, in a transdermal matrix, has been shown to be highly effective in the prevention of motion sickness.[37] For the optimal effect, transdermal scopolamine should be applied 4 hours before the antiemetic effect is required. The patch should be placed on the mastoid process, as it is an effective absorption site. The transdermal scopolamine matrix is designed to release scopolamine at a rate of 5 μg per hour over a 3-day period. A recent study found that prophylactic transdermal scopolamine reduces nausea in patients receiving epidural morphine analgesia after gynecologic surgery.[31] The efficacy of placing a transdermal scopolamine patch prior to surgical delivery in an effort to prevent postpartum nausea and vomiting is currently being evaluated.

Pruritus

Pruritus is a common side effect, and its incidence is greatly dependent on the method of detection. It is generally agreed that most patients admit to some degree of pruritus with bothersome itching, requiring treatment in 25 to 40% of patients. Treatment of pruritus after intraspinal opiates usually involves antihistamines and naloxone. Antihistamines are largely ineffective and can cause sedation.[11] Naloxone is very effective in reducing pruritus, yet is limited by its short duration of action.[39] Its action may acutely reverse analgesia as well.[22]

Nalbuphine, a narcotic agonist/antagonist effectively reverses the pruritus caused by intraspinal morphine[50] and fentanyl.[14] The onset of the relief is evident in 15 minutes, which is somewhat longer than with systemic naloxone, yet the duration of action and relief is significantly longer.[14] Small doses of nalbuphine, 2.5 to 10 mg, injected subcutaneously or intravenously, can provide mild additional analgesia without contributing to respiratory depression. In fact, Doran et al[17] reported that a bolus followed by an infusion of nalbuphine reduced respiratory depression and significantly decreased the elevated $PaCo_2$ resulting from a large dose (0.15 mg per kg) of epidural morphine.

Herpes Simplex Virus Labialis

Recurrent herpes simplex virus labialis has been reported to occur in patients who have received epidural morphine following cesarean section.[12, 20] The mechanism of reactivation of the virus is unknown, yet may be related to mechanical irritation from rubbing and scratching the skin in response to pruritus.

PATIENT-CONTROLLED ANALGESIA

Although the majority of cesarean sections are performed with regional anesthesia in this country, approximately 40% are carried out with general anesthesia. For the woman emerging from a general anesthetic for her cesarean section, self-administered parenteral opiates will aid in her comfort and recovery. PCA is associated with good-to-excellent pain control and high patient acceptance when used for the treatment of postoperative pain.[53] For the surgical patient, the efficacy and safety of this intravenous technique has been well established for the commonly used opioid analgesics morphine and meperidine.[52] This technique has the advantage of allowing for interpatient variability in analgesic requirements, while minimizing the delay between the perception of pain and its relief. Intravenous PCA will allow the parturient to self-administer small doses of analgesic medications as necessary to control postoperative pain.

PCA use does require patient participation. Patients acknowledge and favor an increased sense of control over their care, eliminating the need to negotiate with others for pain medication and relief. Analgesia by PCA allows the parturient to time medication in order to avoid sedation while breast feeding, during interaction with visitors, and with ambulation. Given this control, the patient can balance comfort with the degree of side effects that she is willing to tolerate. In addition, the perception of control can decrease the level of anxiety and further enhance satisfaction with the hospital childbearing experience.

This technique does require the use of an additional medical device. The use of these expensive machines requires comprehensive nursing education and instructional maintenance to avoid unintentional misprogramming, possibly producing narcotic overdose. The machines are bulky and must accompany patients when ambulating. Intravenous access for drug delivery is a necessity. Thorough patient instruction and reinforcement is important to ensure satisfactory participation and analgesia.

Two enlightening studies[19, 24] compare epidural morphine versus intravenous PCA morphine versus intramuscular morphine following cesarean section. Both show that epidural morphine provides the best pain relief with the least amount of drug. Both epidural and PCA morphine provided better pain relief than the traditional intramuscular postoperative analgesia administered as needed. Although the patients who received epidural morphine had the best analgesia, patients who received PCA morphine found it at least as acceptable and perhaps even preferable to epidural morphine. The expressed satisfaction and enthusiasm for PCA analgesia may be related to the immediate accessibility of analgesia and the ability to control side effects.

In this study, Eisenach et al[19] reported two major drawbacks to epidural morphine compared with PCA. First, a bolus of epidural morphine (5 mg of preservative-free morphine in 10 mL of preservative-free normal saline) given after delivery of the infant, does not last 24 hours in all patients. By 12 hours, 40% of the patients require systemic opiate medication. Second, epidural morphine produces a high incidence of bothersome side effects for the parturient. With epidural morphine, there is a 42% incidence of treatable pruritus and 30% incidence of vomiting, compared with 7% and 5%, respectively, with PCA. Despite less complete analgesia, the group of parturients using the PCA were at least as satisfied, it not more satisfied than those patients who received epidural morphine (Table 3).

SUMMARY

In this young and healthy group of patients, exceptional changes have occurred to improve overall maternal and infant outcome. Yet there is still room to improve individual analgesia following cesarean section, improve the satisfaction with the child-bearing experience, and augment the resumption of normal activity. Many recent advances

Table 3. *Comparison of Analgesia for Cesarean Section*

Analgesia	Epidural > PCA > IM
Sedation	PCA ≥ Epidural > IM
Pruritus	Epidural > PCA = IM
Nausea	Epidural > PCA = IM
Satisfaction	PCA ≥ Epidural > IM

Adapted from Chestnut DH: What is new in obstetric anesthesia. International Anesthesia Research Society. Review Course Lectures, 1989.

in pain management directly benefit the parturient during labor, during delivery, and after her cesarean section.

For pain relief during labor, when compared with local anesthetic alone, patients receiving both local anesthetics and low-dose opiates report a more rapid onset of analgesia, more profound analgesia, longer duration of analgesia, and less motor blockade compared with traditional local anesthetic alone. During and following cesarean section, intraspinal opiates, both epidural and intrathecal, provide superior analgesia with tolerable side effects. PCA devices reliably produce sustained pain control with fewer bothersome side effects and are at least equally satisfactory to patients compared with epidural analgesia. In the future, intravenous PCA may deliver improved labor analgesia with insignificant fetal effects accompanied with improved maternal satisfaction. Epidural PCA may receive wider application in the future, both for labor and postoperative analgesia.

New drugs are currently under development. Ongoing investigative efforts aim to anatomically target the action of the drug to specific opiate receptors when administered into the intrathecal and epidural space. The future strives to achieve an intraspinal drug with strong analgesic action without production of neonatal effects, maternal respiratory depression, somnolence, nausea, or tolerance.

REFERENCES

1. Abboud TK, Dror A, Mosaad P, et al: Mini-dose intrathecal morphine for the relief of post-cesarean section pain: Safety, efficacy and ventilatory responses to carbon dioxide. Anesth Analg 67:137–143, 1988
2. Abouleish E: Combined intrathecal morphine and bupivacaine for cesarean section. Anesth Analg 67:370–374, 1988
3. Ackerman WE, Juneja MM, Colclough MD, et al: Epidural fentanyl significantly decreases nausea and vomiting during uterine manipulation in awake patients undergoing cesarean section. Anesthesiology 69:A678, 1988
4. Allen PD, Walman T, Concepcion M, et al: Epidural morphine provides postoperative pain relief in peripheral vascular and orthopedic surgical patients. Anesth Analg 65:165–170, 1986
5. Brodsky JB: Caudal epidural morphine for post-thoracotomy pain. Anesth Analg 67:409–410, 1988
6. Brownridge P, Frewin DB: A comparative study of techniques of postoperative analgesia following cesarean section and lower abdominal surgery. Anaesth Intensive Care 13:123–126, 1985

7. Chadwick HS, Ready LB: Intrathecal and epidural morphine sulfate for postcesarean analgesia—a clinical comparison. Anesthesiology 68:925–929, 1988
8. Chestnut DH: What is new in obstetric anesthesia. International Anesthesia Research Society. Review Course Lectures, 1989, pp 1–6
9. Chestnut DH, Choi WW, Isbell TJ: Epidural hydromorphone for post-cesarean analgesia. Obstet Gynecol 68:65–69, 1986
10. Cohen SE, Woods WA: The role of epidural morphine in the post-cesarean patient: Efficacy and effects on bonding. Anesthesiology 58:500–504, 1983
11. Cousins MI, Mather LE: Intrathecal and epidural administration of opioids. Anesthesiology 61:276–310, 1984
12. Crone LL, Conly JM, Clark KM, et al: Recurrent herpes simplex virus labialis and the use of epidural morphine in obstetric patients. Anesth Analg 67:318–323, 1988
13. Cullen ML, Staren ED, El-Ganzouri A, et al: Continuous epidural infusion for analgesia after major abdominal operations: A randomized, prospective, double-blind study. Surgery October, 718–726, 1985
14. Davies GG, From R: A blinded study using nalbuphine for prevention of pruritus induced by epidural fentanyl. Anesthesiology 69:763–765, 1988
15. Donovan M, Dillon P, McGuire L: Incidence and characteristics of pain in a sample of medical-surgical inpatients. Pain 30:69–78, 1987
16. Donovan BD: Patient attitudes to postoperative pain relief. Anaesth Intensive Care 11:125–129, 1983
17. Doran R, Baxter AD, Samson B, et al: Prevention of respiratory depression from epidural morphine in post-thoracotomy patients with nalbuphine hydrochloride. Anesthesiology 67:A248, 1987
18. Dougherty TB, Baysinger CL, Henenberger JC, et al: Epidural hydromorphone with and without epinephrine for post-operative analgesia after cesarean delivery. Anesth Analg 68:318–322, 1989
19. Eisenach JC, Grice SC, Dewan DM: Patient-controlled analgesia following cesarean section: A comparison with epidural and intramuscular narcotics. Anesthesiology 68:444–448, 1988
20. Gieraerts R, Navalgund A, Vaes L, et al: Increased incidence of itching and herpes simplex in patients given epidural morphine after cesarean section. Anesth Analg 66:1321–1324, 1987
21. Gregory MA, Brock-Utne JG, Bux S, et al: Morphine concentration in brain and spinal cord after subarachnoid morphine injection in baboons. Anesth Analg 64:929–932, 1985
22. Gueneron JP, Ecoffey C, Carli P, et al: Effect of naloxone infusion on analgesia and respiratory depression after epidural fentanyl. Anesth Analg 67:35–38, 1988
23. Gustafsson LL, Schildt B, Jacosen K: Adverse effects of epidural and intrathecal opiates: Report of a nationwide survey in Sweden. Br J Anaesth 54:479–486, 1982
24. Harrison DM, Sinatra R, Morgese L, et al: Epidural narcotic and patient-controlled analgesia for post-cesarean section pain relief. Anesthesiology 68:454–457, 1988
25. Henderson SK, Matthew EB, Cohen H, et al: Epidural hydromorphone: A double-blind comparison with intramuscular hydromorphone for postcesarean section analgesia. Anesthesiology 66:825–830, 1987
26. Hug Jr CC: Pharmacokinetics of new synthetic narcotic analgesics. *In* Estafanous FG (ed): Opioids in Anesthesia. Boston, Butterworth, 1984, p 52
27. Knapp, Writer: SOAP (Society for Obstetric Anesthesia), Annual Meeting, abstract presentation, San Francisco, 1988
28. Leicht CH, Hughes SC, Dailey PA, et al: Epidural morphine sulfate for analgesia after cesarean section: A prospective report of 1000 patients. Anesthesiology 65:A366, 1986
29. Logas WG, El-Baz N, El-Ganzouri A, et al: Continuous thoracic epidural analgesia for postoperative pain relief following thoracotomy: A randomized prospective study. Anesthesiology 67:787–791, 1987

30. Loper KA, Ready LB: Epidural morphine after anterior cruciate ligament repair: A comparison with patient-controlled intravenous morphine. Anesth Analg 68:350–352, 1989
31. Loper KA, Ready LB, Dorman BH: Prophylactic transdermal scopolamine patches reduce nausea in postoperative patients receiving epidural morphine. Anesth Analg 68:144–146, 1989
32. Naulty JS, Datta S, Ostheimer GW, et al: Epidural fentanyl for post-cesarean delivery pain management. Anesthesiology 63:694–698, 1985
33. Neil A, Terenius L: Receptor mechanisms for nociception. *In* Sjostrand UH, Rawal N (eds): Regional Opioids in Anesthesiology and Pain Management. Boston, Little Brown, 1986, p 2
34. Nordberg G, Hedner T, Mellstrand T, et al: Pharmacokinetic aspects of intrathecal morphine analgesia. Anesthesiology 60:448–450, 1984
35. Penon C: Analgesia and ventilatory response to carbon dioxide after intramuscular and epidural alfentanil. Anesth Analg 67:313–317, 1988
36. Premuda L: Historical perspective in opioid analgesia. Satellite Symposium of the 5th World Congress on Pain, Venice, Italy, July 26–28, 1987
37. Price NM, Schmitt LG, McGuire J, et al: Transdermal scopolamine in the prevention of motion sickness at sea. Clin Pharmacol Ther 29:414–419, 1981
38. Rawal N, Arner S, Gustafsson LL, et al: Present state of extradural and intrathecal opioid analgesia in Sweden: A nationwide follow-up study. Br J Anaesth 59:791–799, 1987
39. Rawal N, Schott U, Dahlstrom B, et al: Influence of naloxone infusion on analgesia and respiratory depression following epidural morphine. Anesthesiology 64:194–201, 1986
40. Rawal N: Single segment combined subarachnoid and epidural block for caesarean section. Can Anesth Soc J 33:254–255, 1986
41. Rawal N, Sjostrand U, Christoffersson E, et al: Comparison of intramuscular and epidural morphine for postoperative analgesia in the grossly obese: Influence on postoperative ambulation and pulmonary function. Anesth Analg 63:583–592, 1984
42. Rawal N, Sjostrand U, Dhalstrom B: Postoperative pain relief by epidural morphine. Anesth Analg 60:726–730, 1981
43. Ready LB, Oden R, Chadwick HS, et al: Development of an anesthesiology-based postoperative pain management service. Anesthesiology 68:100–106, 1988
44. Rosen MA, Dailey PA, Hughes SC, et al: Epidural sufentanil for postoperative analgesia after cesarean section. Anesthesiology 68:448–454, 1988
45. Rosen MA, Hughes SC, Shnider SM, et al: Epidural morphine for the relief of postoperative pain after cesarean delivery. Anesth Analg 62:666–672, 1983
46. Shulman MS, Wakerlin G, Yamaguchi L, et al: Experience with epidural hydromorphone for post-thoracotomy pain relief. Anesth Analg 66:1331–1333, 1987
47. Shulman M, Sandler AN, Bradley JW, et al: Post-thoracotomy pain and pulmonary function following epidural and systemic morphine. Anesthesiology 61:569–575, 1984
48. Stenkamp SJ, Easterling TR, Chadwick HS: Effect of epidural and intrathecal morphone on the length of hospital stay after cesarean section. Anesth Analg 68:66–69, 1989
49. Stenseth R, Skellevold O, Breivid H: Epidural morphine for post-operative pain: Experience with 1085 patients. Acta Anaesthesiol Scand 29:148–156, 1985
50. Wakefield RD, Mesaros M: Reversal of pruritus, secondary to epidural morphine, with the narcotic agonis/antagonist nalbuphine (Nubain). Anesthesiology 63:A255, 1985
51. Wang JK, Nauss LA, Thomas JE: Pain relief by intrathecally applied morphine in man. Anesthesiology 50:149–155, 1979
52. White PF: Mishaps with patient-controlled analgesia. Anesthesiology 66:81–83, 1987
53. White PF: Patient-controlled analgesia: A new approach to the management of postoperative pain. Semin Anesth 4:255–266, 1985
54. Yaksh TL, Al-Rodhan NRF, Jensen TS: Sites of action of opiates in production of

analgesia. *In* Fields HL (ed): Progress in Brain Research. New York, Elsevier, 1988
55. Yaksh TL, Rudy TA: Analgesia mediated by a direct spinal action of narcotics. Science 192:1357, 1976
56. Yeager MP, Glass DD, Neff RK, et al: Epidural anesthesia and analgesia in high-risk surgical patients. Anesthesiology 66:729–736, 1987

Address reprint requests to

Joanna Brown Sullivan, MD
Department of Anesthesiology
University of California, San Francisco
521 Parnassus Avenue
San Francisco, CA 94143-0410

Obstetric Anesthesia 0889-8537/90 $0.00 + .20

Recovery Room and Postoperative Complications of Cesarean Section

Richard B. Clark, MD, and Frank C. Miller, MD†*

In the recent past, much progress has been made in the design and staffing of postpartum recovery rooms.[32] As the practice of obstetrics changes, new demands are being placed on the recovery room and its personnel. The traditional postpartum recovery room had as its primary function the close observation of the patient during recovery from anesthesia and the detection of postpartum hemorrhage. Surgical patients were seldom cared for in the traditional postpartum recovery area, because cesarean sections were usually performed in the surgical suite. Post-cesarean section patients were managed in the anesthesia recovery room, which was staffed by recovery room nurses under the primary supervision of the anesthesiologist. The shift to performing cesarean sections in the labor and delivery suite necessitated a change in labor and delivery recovery rooms. Currently, postpartum recovery rooms should be staffed and equipped in the same fashion as acute anesthesia and operative recovery rooms. Such units must be provided with all currently available bedside monitoring equipment as well as life support systems. Nursing personnel must be trained for this intensive care function with special instruction in the hemodynamic adjustments and other physiologic processes peculiar to post-cesarean section patients. Supervision of the postpartum recovery room has traditionally been the function of the obstetric staff. As this function has expanded and become more complicated and sophisticated, many hospitals have gone to an obstetric anesthesia team concept to supervise and manage patients. This new approach offers the patient the safest atmosphere in which to recover and sig-

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From the University of Arkansas for Medical Sciences and the University Hospital, Little Rock, Arkansas

* Professor, Departments of Anesthesiology and Obstetrics and Gynecology; Director, Obstetric Anesthesia

† Professor and Chairman, Department of Obstetrics and Gynecology; Chief of Staff

nificantly reduces the incidence and severity of postoperative complications.

MONITORING EQUIPMENT IN THE RECOVERY ROOM

Recovery rooms must be provided with basic equipment for monitoring vital signs. At the very least, blood pressure, pulse, respiration, and temperature must be followed. All patients should have ECG and blood pressure monitoring during delivery if they are receiving major anesthetics (epidural, spinal, or general); monitoring should be continued during the recovery period. Pulse oximetry has recently become widely available and is to be recommended, particularly for patients recovering from sedation or general anesthesia. In special cases, an arterial line, central venous pressure catheter, and a Swan-Ganz catheter may be utilized.

NURSE TRAINING

Nurses trained to deal with sophisticated monitoring, as well as the usual recovery room expertise in airway management, prevention of aspiration, and arterial hypotension, in addition to the traditional obstetric complications of uterine atony, postpartum hemorrhage, and bladder maintenance, are needed. As this may be expecting too much of one nurse, obstetric nurses may be rotated through the main operating room recovery room to gain these post-anesthetic skills. In our hospital if sophisticated monitoring such as that provided by indwelling arterial catheters, pulmonary artery catheter, and so forth, are deemed necessary, the patient is transferred to an intensive care unit where the intensive care nurse deals with these aspects, while an obstetric nurse cares for the obstetric problems. The converse may also be desirable, that is, an intensive care nurse could assist in care in the obstetric suite.

COMPLICATIONS IN THE RECOVERY ROOM

Regional Anesthesia

Hypotension. Anesthesia complications may arise from the use of regional (spinal, epidural) or general anesthesia. The use of spinal or epidural anesthesia results in significant blockade of the sympathetic nervous system, which can produce systemic vasodilation and arterial hypotension. This usually occurs in the operating room but may be seen in the recovery room as well. Because it is difficult to distinguish from arterial hypotension produced by blood loss, both must be kept in mind. If there has been significant unreplaced blood loss, blood transfusion may be indicated. Measurement of hematocrit and urinary output are helpful in assessing volume status. If the anesthetic alone is thought to be responsible, Trendelenburg's position and a fluid challenge of crystalloid are used and oxygen is given. In the face of a normal blood volume, a vasopressor is administered to maintain blood pressure until sympathetic tone returns. Useful vasopressors are ephedrine (50 mg IM or 15 mg IV) or dopamine (5 to 10 μg per kg per minute IV).

Neurologic Deficits. Neurologic deficits are fortunately quite rare but occasionally present in the recovery room. Failure of a regional anesthetic to wear off has been reported in the past but is virtually unheard of today. This might have been a type of transverse myelitis due to contaminants of the spinal or epidural needles or drug.[9] There have been a few case reports of accidental injection of chloroprocaine into the subarachnoid space, resulting in neurologic impairment. At this institution, we have seen one case of the cauda equina syndrome (loss of bowel and bladder sphincters, perineal anesthesia), which occurred in a male patient. This followed an uncomplicated spinal anesthetic, and to our knowledge, never resolved.

Epidural abscess and epidural hematoma are quite rare in the obstetric population. The former would be characterized by back pain, fever, and evolving neurologic signs (weakness of the lower extremities).[5] Most epidural abscesses result from endogenous spread, rather than by contamination by spinal or caudal injection.[5] Treatment is by antibiotic administration and surgical drainage. Epidural hematomas are characterized by pain in the back or legs or progressive weakness of the legs.[5] Modern imaging techniques can assist in making a rapid diagnosis. Urgent laminectomy should be performed if there are any clinical or radiologic signs of spinal cord compression.[5] Epidural hematoma may occur spontaneously but is more likely to occur in conjunction with major regional anesthesia if the patient is anticoagulated.

Neurologic deficits in the recovery room may also have resulted from surgical trauma, improper positioning of the patient during surgery, retractors, or pressure on the lumbosacral plexus by the fetal head.

This last complication ("obstetric paralysis") occurs in approximately 1:2500 deliveries and may be confused with or attributed to a lesion produced by regional anesthesia. The neurologic symptoms, which appear 24 to 48 hours after delivery, are usually limited to the distribution of the common peroneal nerve, the obturator nerve, or both, and vary from paresthesia to complete anesthesia, and from paresis to the total paralysis of the respective muscles. Usually complete recovery occurs after a length of time, which may last up to 6 months.[4]

Apnea Due to Epidural or Intrathecal Narcotics. The epidural and subarachnoid administration of a narcotic, such as morphine, has recently become quite popular for postoperative pain relief. Postoperative analgesia is usually excellent for up to 24 hours, allowing for early ambulation. There is a slight chance of a delayed onset of respiratory depression or apnea with this technique. This has been reported in obstetric patients.[24] Vital signs, particularly respiration, should be monitored frequently during this period. In addition to determining respiratory rate at hourly intervals for 24 hours, an apnea monitor may also be considered. Utilization of a sedation score is extremely useful for identifying patients at risk for respiratory depression.

General Anesthesia

Soft-Tissue Obstruction. General anesthesia can be associated with a variety of complications, many of which are seen in the recovery room. If the patient is still unconscious when brought to recovery, there may be soft-tissue obstruction, particularly if the tongue falls against the posterior pharynx, producing upper-airway obstruction. Unconscious patients should be kept on their side to reduce the chance of soft-tissue obstruction. This also reduces the chance of aspiration should vomiting or regurgitation occur. Post-cesarean section patients should virtually never be unconscious in the recovery room unless an endotracheal tube is in place.

Pregnant patients are known to have congestion of the nasopharynx, larynx, trachea, and bronchi. This predisposes to nose bleed during nasotracheal intubation and to a reduction in airway diameter. A pregnant patient usually requires an endotracheal tube of smaller diameter than is used for the nonpregnant patient, that is, a 7.0-mm outside diameter versus 8.0-mm tube. The hyperemia usually present in the airway is exaggerated in the preeclamptic patient and is associated with edema of the nasal passages, pharynx, larynx, trachea, and bronchi. Post-extubation airway obstruction due to laryngeal edema may occur. Pharyngolaryngeal edema without airway obstruction can also be a presenting symptom in preeclampsia. The airway must be kept open, by oropharyngeal airway, endotracheal tube, or tracheotomy, depending on each specific case.

Hypoventilation. Alveolar hypoventilation with resultant hypoxemia is common in the recovery room, because many drugs producing respiratory depression are employed during both general and regional anesthesia. Oxygen by nasal cannula or mask has been given routinely in the surgical recovery room and should be used in the obstetric recovery room as well. Narcotics, benzodiazepines, and muscle relaxants are among the drugs most likely to cause problems. Even though the newer narcotics (fentanyl, sufentanyl) have a short duration of action, they can produce hypoventilation. If inadequate respiration is suspected, respiratory rate, tidal volume, and vital capacity can be measured. Pulse oximetry is a quick and noninvasive means of detecting hypoxia before it is clinically significant and should be used for virtually all patients in the recovery room. Arterial blood gases may also be checked. If the patient has received narcotics, either in large quantities or near the end of surgery, naloxone or nalbuphine can be given intravenously by careful titration. One must keep in mind that naloxone has a short duration of action and the narcotic effect may outlast the narcotic antagonist, so the dose may have to be repeated.

The effect of muscle relaxants such as pancuronium, curare, and even succinylcholine may persist into the recovery room. Tidal volume and minute volume give an idea of respiratory adequacy, but inspiratory force, the head lift determination (at least 5 seconds), and the use of a nerve stimulator are more diagnostic. If residual block is revealed by the nerve stimulator, reversal with neostigmine and glycopyrrolate or edrophonium and atropine may cure the problem. If the block is too profound and reversal is inadequate, re-intubation and maintenance on a ventilator can support the patient until the neuromuscular block has dissipated. Magnesium sulfate will potentiate both depolarizing and nondepolarizing neuromuscular blocking drugs. This may be difficult to reverse, although calcium chloride may help. Although rare in the recovery room, high spinal or epidural anesthesia (sensory level T_4 or higher) can cause hypoventilation. This may be augmented by sedatives or narcotics administered intraoperatively. Treatment depends on the degree of respiratory embarrassment. Minor hypoventilation can be treated with an oxygen mask. If there is evidence of significant hypoventilation, respiration may need to be assisted and an endotracheal tube may need to be inserted.

Aspiration. The aspiration of gastric contents has been a major concern of obstetric anesthesiologists for many years. Aspiration may not be recognized in the operating room and become manifest in the recovery room. It also may occur in the recovery room. Patients may aspirate particulate gastric contents or acidic gastric secretions. Because the acidity of the aspirated gastric contents influences the severity of aspiration-pneumonitis, ingestion of an oral antacid (sodium citrate) prior to general anesthesia for obstetric procedures is indicated. The use of cimetidine, ranitidine, and metoclopramide is currently being evaluated.

If pulmonary aspiration does occur, the patient is placed in Trendelenburg's position, and the mouth, pharynx, and trachea are suctioned. If the aspirate from the trachea has a pH of less than 2.5 and a volume of 25 mL or greater an intense pulmonary reaction is inevitable because this is the critical pH for the development of this form of respiratory distress syndrome. It is not unusual to have to intubate the patient's trachea and institute mechanical ventilation. When a chest roentgenogram is taken, the superior segment of the right lower lobe is most likely to be involved if the patient was supine.[9] Therapy includes judicious use of IV fluids, bronchodilators for bronchospasm, and mechanical ventilation. Antibiotics should be used only if there is infection. Steroid therapy remains controversial but is probably of limited or no value.

Mechanical ventilation with positive end-expiratory pressure is the most important aspect of the treatment. Early institution affects mortality more than any other step.[9] Mechanical support of ventilation is employed if the patient has a PO_2 of less than 70 mm Hg on 40% O_2, an alveolar-arterial oxygen difference of greater than 140 on 40% 0_2, or a shunt greater than 15%; it may be used prophylactically if the gastric contents are acidic (pH less than 2.5) or acid secretions have been aspirated from the bronchial tree.[9] Positive pressure ventilation is administered with 5 to 10 cm H_2O positive end-expiratory pressure (PEEP). Intermittent manditory ventilation is usually employed. Management is then directed by blood gas data. PEEP is adjusted to keep the alveolar arterial oxygen difference on 40% O_2 less than 140 mm, or shunt less than 15%.

POSTPARTUM COMPLICATIONS

Pulmonary

Aspiration. Although anesthetic problems would be expected to manifest themselves in the intraoperative period or in the recovery phase, aspiration pneumonitis may be first detected in the postpartum period.

Atelectasis. Atelectasis is caused by shallow breathing, secretions, and hypoventilation from narcotics. It can result in hypoxemia, hypercarbia, and fever. Mild atelectasis may not be apparent on a chest roentgenogram but can result in hypoxemia. It may also be profound enough to cause lobar collapse or even collapse of a whole lung, with mediastinal shift. A vigorous "stir-up" regimen in the postoperative period is the best prevention and treatment. Atelectasis is the most common cause of apparent right-to-left shunt and hypoxemia in the post-anesthetic period.[26]

Embolus. The pregnant patient is at increased risk for deep vein thrombosis and pulmonary thromboembolism because of the hypercoaguable state during gestation and vena caval obstruction. Pulmonary thromboembolism in the postpartum period can result in severe respiratory distress because the alveoli are ventilated but not perfused, resulting in hypoxemia and either hypercarbia or hypocarbia if there is hyperventilation. Treatment is usually directed at maintaining oxygenation and preventing further thrombus by heparinization. Pulmonary embolus from dislodgement of clots usually occurs after discharge from the recovery room, but may occur intraoperatively or in the recovery period. It is usually diagnosed by the clinical picture of chest pain, tachypnea, dyspnea, and tachycardia as well as laboratory examination (arterial blood gases show hypoxemia and hypocarbia, ventilation-perfusion scans and pulmonary angiography demonstrate the obstruction in the pulmonary circulation.

Amniotic fluid embolism usually occurs during labor or at the time of delivery, but may manifest itself some time post delivery. Dyspnea, cyanosis, cardiovascular collapse, coma, coagulopathy, and occasionally, pulmonary edema, are seen. The treatment is strictly supportive. Prompt and aggressive intervention has reduced the mortality rate of this serious complication.

An air embolus occurs when air enters the venous system, and is occasionally seen during cesarean section or gynecologic surgery in Trendelenburg's position when the operative site is higher than the heart. This can be identified by Doppler ultrasonic methods (most sensitive), a decrease in the end tidal CO_2level, or the appearance of a mill wheel murmur over the precordium. This last method is the least sensitive and occurs just before cardiovascular collapse. The preferable treatment is aspiration of the air from the vascular tree, but if this is impossible the field is flooded with sterile saline, the point of entry is closed, and the patient placed in the head-down, right-side-up position. Oxygen is administered. Support of the circulation by cardiopulmonary resuscitation or vasopressors may be necessary.

Neurologic

Spinal Headache. Probably the most common neurologic complication related to anesthesia in the postpartum period is the post–dural-puncture headache. This headache is the result of cerebrospinal fluid leakage and is caused by in sagging of the brain and pain-sensitive structures (blood vessels, tentorium), producing the headache.[8] It is thus a low pressure headache. The incidence is related to the needle size, gender, and age, and can range from 0.2% with a 25-gauge puncture to greater than 50% with an 18-gauge puncture.[4] Our incidence for obstetric patients with a 22-gauge needle is 11%. The incidence is lowest in males over 60 years of age and highest in obstetric patients. It is not known whether this propensity for post-puncture headache is due to the pregnant state or to the fact that the patient is a young female.

The main diagnostic criterion of spinal headache is its postural nature. Symptoms are exacerbated by the upright position and relieved when recumbent. The location of the cephalgia may vary (frontal, occipital, parietal) and is nondiagnostic.[9] The headache usually becomes apparent 1 to 5 days after the lumbar puncture and characteristically persists for 3 to 5 days or longer. Rarely, it lasts for months.[1,2] Bedrest after a dural puncture does not reduce the incidence of spinal headache, so early ambulation is not contraindicated.[23]

The treatment of post-spinal headache is mainly directed toward returning the cerebrospinal fluid pressure to normal. Fluids (3000 mL per day by mouth or intravenously) are administered.[27] Bedrest and analgesics (for example, aspirin, codeine) reduce the patient's suffering until the headache is gone. An abdominal binder has been recommended to obstruct the inferior vena cava and raise cerebrospinal fluid pressure.[27] If these are ineffective, caffeine and sodium benzoate (500 mg) may be given intravenously.[30,31] If the headache persists, the dose may be repeated in 8 hours. Supposedly, cerebral blood vessels are dilated with spinal headache, and the caffeine constricts them. We have had a success rate of about 50% with this therapy.[8] Others have found it more efficacious.[22]

The definitive treatment of post–dural-puncture headache is the restoration of cerebrospinal fluid pressure by the installation of a fluid into the epidural space, which compresses the dura. Several investigators have reported the use of saline. Craft et al[11] found that two 60-mL injections of normal saline into the epidural space after unintended dural puncture reduced the headache rate from 76.5 to 12.5%. A more lasting result is obtained with the epidural blood patch; here the headache is not only cured immediately, but does not usually recur due to the sealing of the dural hole by the blood clot. First described by Gormley[20] and popularized by DiGiovanni,[12] this technique has been universally acclaimed.[33] Our success rate is about 95%. What of administering an epidural blood patch before the headache appears? The work of Loeser et al[25] would indicate prophylactic blood patching would be fruitless; if administered within 24 hours of puncture, they found that the success rate for treatment of headache was only 29% (10 mL autologous blood). Palahniuk et al [29] when faced with an unintentional dural puncture repeated the epidural at another interspace, inserted an epidural catheter, and proceeded with the anesthetic. Before removing the epidural catheter, 10 mg of autologous blood were injected. Their results were poor. However, more recent investigators[9a] using larger volumes of blood through the epidural catheter are achieving better results. Perhaps prophylactic administration of blood will be effective if larger volumes are used.

Infection. Bacterial meningitis is extremely rare after spinal anesthesia. It should not occur if adequate precautions are taken. An exception might be meningitis from transient bacteremia, unrelated to the anesthesia.

POSTOPERATIVE COMPLICATIONS

Of all post-cesarean section complications, infection is by far the most common. The Obstetrical Statistical Cooperative[10] reported puerperal complications following cesarean birth in order of frequency. The three most common complications were endometritis, pyelonephritis, and wound infection. These were followed by urinary tract injury and infection, respiratory complications, hemorrhage, and post-anesthesia complications. More recently, Nielsen and Hokegard[28] of Sweden reported their experience with cesarean section in more than 1300 cases (Table 1). They reported postoperative complications as minor or major. Minor complications constituted 11.5% of their more than 1300 cesarean sections. Of those, infection made up 98% of the complications, with paralytic ileus occurring in 3 of 152 cases. Of the major complications, again infection was the most common with perimetritis or peritonitis and pneumonia being the most frequent. Pelvic abscess or infected hematoma and intra-abdominal hemorrhage were the next most common complications. Bladder injury and delayed hemorrhage were reported but far less frequently.

Infection

Pelvic infection is the most common puerperal complication following cesarean section. The incidence of myometritis in these women ranges from 5 to 85% and is related to multiple factors.[19] Of these, the duration of ruptured membranes, duration of labor, number

Table 1. *Rate and Type of Major Postoperative Complication after 1319 Cesarean Sections*

COMPLICATION	NO. OF PATIENTS
Reoperation because of intra-abdominal hemorrhage	4
Reoperation because of pelvic abscess or infected hematoma	8
Parametritis and peritonitis	12
Pneumonia	6
Bladder paresis and urethral catheter > 5 days	2
Severe paralytic ileus > 5 days	2
Thrombosis	1
Pneumothorax	1
Delayed hemorrhage with shock	1
Sepsis	1
Hysterectomy caused by bleeding in uterine scar	1
Total	39 (3.0%)

Adapted from Nielsen TF, Hokegard KH: Postoperative cesarean section morbidity: A prospective study. Am J Obstet Gynecol 146:911, 1983.

of vaginal examinations, and socioeconomic status are the most frequently associated risk factors. Nielsen and Hokegard[28] reported the highest puerperal complication rate in patients with ruptured membranes lasting greater than 16 hours and the presenting part of the fetus at or below the ischial spine. The extent to which obesity, general anesthesia, or anemia influence the incidence of pelvic infection remains unproved.

Microbiology. Endometritis is most often due to a mixed infection with anaerobic and aerobic bacteria in approximately equal proportions (54% aerobic, 46% anaerobic).[17] An average of 2 to 3 microorganisms will be recovered from endometrial cultures. The most common bacteria are the aerobic organisms. *Escherichia coli* is the most common gram-negative and *Streptococci* is the most common gram-positive organism. Anaerobic organisms are recovered more frequently and have a major role in postpartum infections. The most common is the *Bacteroides* species (gram-negative bacilli). In order of frequency they are *Bacteroides fragilis, Bacteroides bivius,* and anaerobic *Streptococci.*

Postpartum Endomyometritis

Diagnosis. The earliest manifestation of pelvic infection is metritis with pelvic cellulitis, secondary to bacterial invasion of the myometrium with spread along the tissue planes to lymphatic and venous supplies within the broad ligaments. Symptoms include (1) fever, (2) uterine tenderness, and (3) purulent or foul lochia. Nonspecific symptoms such as malaise, chills, and tachycardia may also be present. Laboratory studies should include (1) complete blood count, (2) uterine culture and Gram stain genital culture, and (3) two venous blood cultures.

Contamination is a major problem when attempting an endometrial culture. Cultures taken from the vagina endocervix may not reflect the flora of the endometrial cavity. Blood cultures may be helpful, because approximately 10 to 20% of patients may have bacteremia. The presence of bacteria in blood cultures does not necessarily imply that the endometritis is a result of the isolated bacteria. Therefore, therapy directed solely against these isolates may be inappropriate.

Therapy. When post-cesarean section myometritis occurs, early therapy with intravenous antibiotics is indicated. Because therapy should be initiated before culture results have been obtained, the initial therapy is empiric. As previously discussed, the number and diversity of potential pathogens would dictate that therapy should be "broad spectrum." Since the majority of clinical bacterial infections result from anaerobes, the therapeutic regimen should include penicillin or a penicillin-like drug. In separate studies, Gibbs et al[18] and DiZerega et al[13] reported cure rates ranging from 65 to 78% with penicillin plus an aminoglycoside or penicillin plus tetracycline. Failures were usually due to resistant organisms, primarily *Bacteroides fragilis.* DiZerega and colleagues[13] evaluated the combination of clindamycin and gentamycin in post-cesarean section patients from LAC/USC Medical Center and reported a 95% efficacy rate. Others have found similar effectiveness.[17] Since initial therapy for endometritis after cesarean section should consist of broad-spectrum antibiotics with activity against all the *Bacteroides* species as well as gram-positive and gram-negative aerobes, a combination of clindamycin and an aminoglycoside should be the standard therapy. When antibiotic therapy fails, one must consider the possibility of wound infection, pelvic hematoma or abscess, septic pelvic thrombophlebitis, or a noninfectious source.

Septic Pelvic Thrombophlebitis

Pelvic vein thrombophlebitis is a relatively rare obstetric complication. The overall incidence following cesarean section is reported to be approximately 1 to 2% in women with post-cesarean endometritis.[14] The most common organisms associated with septic pelvic thrombophlebitis are anaerobic *Streptococci, Proteus* species, aerobic *Streptococci, Staphylococci,* yeast, and *Bacteroides.*

Diagnosis. Since septic pelvic thrombophlebitis is an uncommon complication of cesarean section, a high index of suspicion enhances the diagnosis. The diagnosis should be suspected in any patient with soft-tissue, pelvic infection, and an elevated temperature despite appropriate antibiotic therapy. The initial physical examination is usually consistent with endomyometritis or pelvic cellulitis. Pelvic vein thrombophlebitis will present in two distinct fashions. The first is acute ovarian vein thrombosis with mild to moderate temperature elevation and lower abdominal pain. This presentation is difficult to differentiate from endomyometritis. However, after appropriate antibiotic therapy, these patients may have persistent fevers with chills and localized abdominal pain, subsequent nausea or vomiting, and abdominal distention. They may appear acutely ill with rapid pulse, tachycardia, and stridor. The symptoms may be easily confused with pulmonary embolism. The frequency of pulmonary embolism as a complication of pelvic vein thrombophlebitis makes the diagnosis more difficult. On pelvic examination, one may find a rope-like, tender abdominal mass in one-half to two-thirds of patients. The mass usually originates near the uterine cornua and extends laterally.[6] The second presentation, which is less distinct, is sometimes referred to as enigmatic fever.[15] These patients usually have responded to initial antibiotic therapy for a diagnosis of postoperative endomyometritis, yet have recurrent temperature spikes as high as 103 to 104 degrees Fahrenheit. Few of these patients will have palpable masses, and diagnosis must be made largely on the basis of clinical history and lack of other physical findings. Diagnosis may be aided by use of an intravenous pyelogram, which may show distinct concentric narrowing of the proximal ureter. Other diagnostic modalities of value include venography, gallein scan, computed tomographic scan, sonogram, and ventricular-perfusion scans.

Treatment. Therapy for septic pelvic thrombophlebitis includes broad spectrum antibiotics and anticoagulation. Initially, intravenous heparin is required for at least 7 to 10 days. Surgery is reserved for patients who do not respond to this therapy. Surgical procedures that have been recommended include bilateral ovarian vein ligation and inferior vena cava ligation or unilateral ovarian vein ligation with or without inferior vena cava ligation.

Urinary Tract Infections

The incidence of urinary tract infections following cesarean section ranges from 1.8 to 16%.[16,17] The most common etiologic organism for post-cesarean section urinary tract infection is *Escherichia coli*, although other gram-negative organisms are not uncommon. The diagnosis of urinary tract infection following ceasarean section is associated with the duration of labor and the difficulty of the delivery. Trauma to the bladder is more common when the fetal presenting part is well engaged in the pelvis. During the early puerperium, the bladder has a greater capacity and is less sensitive to intravesicular fluid tension than in the nonpregnant state. If the urinary catheter is removed and the patient not encouraged to empty her bladder frequently, incomplete emptying and residual urine increase the likelihood of urinary tract infection. Regional anesthesia may predispose to urinary retention in the noncatheterized patient.

Hemorrhage

Postoperative hemorrhage is a well-recognized but relatively infrequent complication of cesarean deliveries. The two most common causes of hemorrhage are uterine atony and intra-abdominal bleeding due to inadequate surgical hemostatis. Lacerations of the genital tract or inadequate surgical hemostasis may lead to profuse vaginal bleeding, which at times is difficult to differentiate from the blood loss of uterine atony. Post-cesarean section uterine atony is related to the same factors as with vaginal birth, that is, prolonged labor, uterine distension secondary to hydramnios or multiple gestation, infection, and tocolytics such as magnesium sulfate or the beta sympathomimetics.

Diagnosis. The diagnosis of hemorrhage secondary to uterine atony is made from palpation of the uterine fundus, which will be enlarged, soft, and boggy. Vaginal examination must be performed to rule out cervical or vaginal lacerations. The cervix, lower uterine segment, or the uterine incision should be explored, because copious bleeding may occur from inadequate hemostasis in the uterine incision or from extensions or lacerations in the lower uterine segment.

Management. Intravenous oxytocin should be supplemented with ergonovine maleate or methylergonovine maleate administered intravenously or intramuscularly.

Uterine atony that does not respond to the usual therapy of intravenous oxytocin or ergotamines may respond to prostaglandin. Prostaglandin was first recommended for pharmacologic therapy of postpartum uterine atony by Buygdeman et al in 1965.[7] Prostaglandin $F_2\alpha$ analogues may be given intramuscularly or directly into the myometrium. Recommended intramuscular or intramyometrial doses are 0.25 mg (one ampule) repeated in 1.5 hours, if necessary.[35]

The prostaglandin $F_2\alpha$ analogue [15-(S)-15-methylprostaglandin $F_2\alpha$] is reported to be more potent and have longer effectiveness than other analogues. The effectiveness of prostaglandins where other oxytocic agents fail could be attributed to the marked idiotropic action or the longer duration of forceful contractions produced by a single injection of prostaglandin. Side effects of prostaglandin include headache, nausea, diarrhea, increased blood pressure, and, in some cases, mild temperature elevation.

Blood and fluid replacement should be begun immediately, since the amount of blood loss is almost always greater than is first estimated. Delay not infrequently results in hypotension, inadequate tissue perfusion, and shock. Coagulation disorders may also result from excessive blood loss. Consumption coagulopathy may be diagnosed by (1) clot observation test, which is the failure of blood clot formation in a test tube or initial clot and subsequent lysis; (2) a decreased platelet count; (3) decreased fibrinogen; (4) increased fibrin split products; (5) prolonged prothrombin time; and (6) prolonged partial thromboplastin time. Transfusion of whole blood is the first choice in treating acute hemorrhage. If whole blood is not available, then packed cells, saline, or fresh frozen plasma may be used. Platelets and cryoprecipitate may be necessary to correct a coagulopathy. In cases of massive hemorrhage and subsequent disseminated intravascular coagulation, fresh whole blood replacement is the most efficient form of replacement therapy, but is increasingly difficult to obtain.

The anesthesiologist will occasionally be called upon to provide anesthesia for re-operation after cesarean section. General anesthesia is most often the choice. If at all possible, the blood volume should be restored to normal before induction. Component therapy may be necessary if a clotting defect exists. Several large intravenous catheters are desirable as massive transfusion may be necessary. Central venous pressure measurement can be a very useful guide to the adequacy of transfusion. The patient should be assumed to have a full stomach and clear antacids, and H_2 antagonists should be administered prior to induction of anesthesia. Cricoid pressure and rapid sequence induction and intubation should be used. Ketamine or etomidate may be preferable to thiopental for induction of anesthesia in the hypovolemic patient. A warming blanket should be placed on the operating table and the temperature of the patient closely watched. Blood and intravenous fluids should be warmed.

Urinary Tract Injury

With the increasing trend away from operative vaginal deliveries, surgical bladder injury has become more common in obstetric practice. Direct bladder injury during cesarean section occurs most often with the dissection of the posterior bladder wall off of the lower uterine segment.

Ureteral injury occurs most often when there is some anatomic distortion such as cervical myomata or pelvic adhesions or scarring. At times when the bladder flap has not been developed, the ureter or bladder may be caught in a clamp or suture during repair of the uterine incision.

Unrecognized bladder-ureteral injury is rare. Barclay[3] reported a 5% incidence of bladder injury and fistula formation with cesarean hysterectomy.

Urinary leakage in the early puerperium is a common presenting symptom. A bladder fistula can be demonstrated by installation of methylene blue via a urethral catheter and leakage observed per vagina. In most cases, adequate bladder drainage will allow for spontaneous closure of the fistula. Drainage should be maintained for about 4 weeks[34] after the patient is completely dry.

SUMMARY

Complications of cesarean section may appear at any time following the initiation of anesthesia. Immediate post-anesthetic complications include drug-induced hypoventilation, aspiration pneumonitis, atelectasis, obstruction of the respiratory tract, neurologic deficits, and hypotension. Embolus and hemorrhage may be manifested in the recovery room. It is as important to provide expert nursing and physician care and equipment in the obstetric recovery room as it is in the surgical recovery room; immediate detection of complications is vital. Infection is the most common complication of cesarean section and is a major problem in approximately 2% of patients. This includes endometritis, pyelonephritis, and wound infection. Bacterial infection involves both aerobes and anaerobes. Specific diagnosis is made from endometrial, wound, and blood cultures, but therapy is started with broad-spectrum antibiotics pending the results of cultures. Upon diagnosis specific therapy is instituted. Anticoagulation is necessary for patients with septic pelvic thrombophlebitis. Patients with urinary tract injury or hemorrhage may require re-operation. Those with clotting defects or hypovolemia should be treated before re-operation, if possible.

REFERENCES

1. Abouleish E: Epidural blood patch for the treatment of chronic post lumbar-puncture cephalgia. Anesthesiology 49:291, 1978
2. Abouleish E, De Le Vega S, Bundinger I, et: Longterm follow-up of epidural blood patch. Anesth Analg 54:459, 1975
3. Barclay DL: Cesarean hysterectomy: Thirty years experience. Obstet Gynecol 35:120, 1970
4. Bonica JJ: Principles and Practice of Obstetric Analgesia and Anesthesia. Philadelphia, Davis, 1969, p 1094
5. Bromage PR: Epidural Analgesia. Philadelphia, Saunders, 1978, p 682
6. Brown TK, Munsick RA: Puerperal ovarian vein thrombophlebitis: A syndrome. Am J Obstet Gynecol 109:263, 1971
7. Buygdeman M, Kwon SU, Mukherjee T, et al: Effect of intravenous infusion of prostaglandin E_1 and E_2 on mortality of the pregnant human uterus. Am J Obstet Gynecol 102:317, 1965
8. Clark RB: Conduction Anesthesia. Clin Obstet Gynecol 24:601–617, 1981
9. Clark RB, Seifen AB: Complications of obstetrical anesthesia. Semin Anesth 1:155, 1982

9a. Colonna RP, Shapiro BE: Unintentional dural puncture and prophylactic epidural blood patch in obstetrics. Anesth Analges 69:522–523, 1989

10. Consensus Development Conference on Cesarean Section, Draft Report of the Task Force on Cesarean Section. U.S. Dept. of Health and Human Services, Public Health Services, National Institute of Health, September 1980
11. Craft JB, Epstein BS, Coakley CS: Prophylaxis of dural puncture headache with epidural saline. Anesth Analg 52:228–231, 1973
12. DiGiovanni AJ, Galbert MW, Wahle WM: Epidural injection of autologous blood for postlumbar-puncture headache. II. Additional clinical experiences and laboratory investigation. Anesth Analg 51:226–232, 1972
13. DiZerega G, Yonekura L, Roy S, et al: A comparison of clindamycin-gentamicin and penicillin-gentamicin in the treatment of post-cesarean section endomyometritis. Am J Obstet Gynecol 134:238, 1979
14. Duff P, Gibbs RS: Pelvic vein thrombophlebitis: Diagnostic dilemma and therapeutic challenge. Obstet Gynecol Surv 38:365, 1983
15. Dunn LJ, VanVorrhis LW: Enigmatic fever and pelvic thrombophlebitis. N Engl J Med 276:265, 1969
16. Farrell SJ, Anderson FH, Work BA: Cesarean section: Indications and postoperative morbidity. Obstet Gynecol 56:696, 1980
17. Gibbs RS, Blanco JO, Castaneda YS, et al: A double-blind randomized comparison of clindamycin-gentamicin vs. cefamandole for treatment of postcesarean endomyometritis. Am J Obstet Gynecol 144:261, 1982
18. Gibbs RS, Jones PM, Wilder CJ: Antibiotic therapy of endometritis following cesarean section. Obstet Gynecol 52:31, 1978
19. Gilstrap LC, Cunningham FG: The bacterial pathogenesis of infection following cesarean section. Obstet Gynecol 53:545, 1979
20. Gormley JB: Treatment of postspinal headache. Anesthesiology 21:565–566, 1960
21. Heller PJ, Scheider EP, Marx GF: Pharyngolaryngeal edema as a presenting symptom in pre-eclampsia. Obstet Gynecol 62:523, 1983
22. Jarvis AP, Greenwalt JW, Fagraeous L: Intravenous caffeine for postdural puncture headache. Reg Anesth 11:42, 1986

23. Jones RI: The role of recumbency in the prevention and treatment of postspinal headache. Anesth Analg 53:733, 1974
24. Leicht CH, Hughes SC, Dailey PA, et al: Epidural morphine sulfate for analgesia after cesarean section: A prospective report of 1000 cases. Presented at Annual Meeting of Society for Obstetric Anesthesia and Perinatology (SOAP), Salt Lake City, Utah, May 17, 1986
25. Loeser EA, Hill GE, Bennett GM, et al: Time vs. success rate for epidural blood patch. Anesthesiology 49:147–148, 1978
26. Miller RM: Anesthesia, ed 2. New York, Churchill Livingstone, 1986, p 1927
27. Moore DC: Anesthetic techniques for obstetrical anesthesia and analgesia. Springfield, IL, Charles Thomas, 1964
28. Nielsen TF, Hokegard KH: Postoperative cesarean section morbidity: A prospective study. Am J Obstet Gynecol 146:911, 1983
29. Palahniuk RJ, Cumming M: Prophylactic blood patch does not prevent postlumbar puncture headache. Can Anaesth Soc J 26:132–133, 1979
30. Sechzer PH, Abel L: Post-spinal anesthesia headache treated with caffeine. Curr Ther Res 24:307, 1978
31. Sechzer PH: Postspinal headache treated with caffeine. Part II: Intracranial vascular distention, a key factor. Curr Ther Res 36:440–448, 1979
32. Shnider SM: The anesthesiologist views the design and function of the delivery room. Anesthesiology 31:172, 1969
33. Shnider S, Levinson G: Anesthesia for Obstetrics. Baltimore, Williams & Wilkins, 1978, p 165
34. Tedford GE, Tanning JD, Slate WG, et al: Pregnancy and extrophy of the urinary bladder. Obstet Gynecol 28:254, 1966
35. Toppozada M, El-Bossaty M, El-Rahman HA, et al: Control of intractable atonic postpartum hemorrhage by 15 methylprostaglandin $F_{2}\alpha$. Obstet Gynecol 58:327, 1981

Address reprint requests to

Richard B. Clark, MD
Department of Anesthesiology
University of Arkansas for Medical Sciences
4301 West Markham
Little Rock, AR 72205

Obstetric Anesthesia 0889–8537/90 $0.00 + .20

AIDS

Concerns for the Obstetric Care Provider

*Cathy Jo Cantrell, MD**

Until recently, obstetricians and women's health care providers have not been greatly concerned about AIDS because they believed that it did not impact greatly on their patients. Clearly, with recent serologic surveys suggesting there will be more than 26,000 cases of AIDS in women by 1991, human immunodeficiency virus (HIV) related illness is now a concern of great magnitude for every clinician.[31]

AIDS and HIV infection, more than any other sexually transmitted disease, require of the care-giver a fund of knowledge that extends beyond medical concerns. It is important for all members of the health care team to understand the impact of this infection on the pregnant woman and her fetus. Clinicians who render primary and specialized obstetric and pediatric care should know how to use and interpret various diagnostic tests presently available and learn how to educate and counsel women who are infected or at risk. All persons who care for seropositive women and infants should familiarize themselves with currently recommended management guidelines as well as therapeutic limitations of this disease. Finally, all who render care to these women are obliged to consider the diverse psychosocial, ethical, and legal issues implicit in the decisions they make. There are yet unresolved problems related to patient confidentiality, notification of sexual partners, patient counseling and education regarding pregnancy risks and pregnancy termination, screening programs, experimental treatment protocols and, lastly, the protection and rights of exposed health care workers.

HIV INFECTION AND AIDS

Epidemiology

AIDS was first reported in the United States in 1981 in homosexual men. In 1983 it became apparent that the sexual partners of men with AIDS were also at risk for developing the disease and that pregnant women could transmit the virus to their fetus.[41] Currently, 2.5 million people are estimated to have been infected with the virus in the United States.[8] It is important to note that AIDS patients make up a small minority of the HIV-infected population and that for each diseased patient there are probably 30 asymptomatic infected individuals. By the end of 1988, women made up only 7% of AIDS patients, but recent data indicate that they comprise a greater percentage of all HIV-seropositive individuals.[7, 26] Thus, by the year 1991, it is likely that nearly 10% of all AIDS cases will be women.[31]

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*Assistant Clinical Professor, Department of Reproductive Medicine, Division of Perinatal Medicine, University of California San Diego, San Diego, California

AIDS and HIV infection occur primarily among homosexual and bisexual men, intravenous (IV) drug abusers and their partners, recipients of multiple blood transfusions and blood products, and individuals from Haiti and Central Africa. More than 50% of the cases of AIDS in the United States have been reported from New York City, Newark, Miami, San Francisco, and Los Angeles, but virtually all major U.S. cities have reported cases. AIDS in children occurs primarily as a perinatal infection (80%).[33] In the majority of these cases, the mothers are either IV drug users or the sexual partners of men who use IV drugs. The other main risk group for children is made up of those who received blood or blood products between 1978 and 1985 (20%). With the advent of HIV screening of all blood products, the risk of transfusion-related AIDS in infants and childen in the United States should almost be eliminated.

Pathophysiology

In 1984, investigators at the National Institutes for Health isolated a retrovirus that they termed the human T-lymphotrophic retrovirus, type III (HTLV-III), which has subsequently been redesignated as HIV.[17] Retroviruses are RNA viruses that contain an enzyme (reverse transcriptase) that transcribes DNA from RNA, a process used in the replication of these viruses. Although retroviruses infect many animal species, only two other retroviruses are known to infect humans. HIV, like other human retroviruses, primarily affects the lymphocytes derived from the thymus (T-lymphocytes), which are responsible for cellular immunity. The AIDS virus preferentially infects the subset of T-lymphocytes known as helper T-lymphocytes, which augment the immune response. The subset of T-lymphocytes that suppresses the immune response, the suppressor T-lymphycytes, is relatively spared. The bone-marrow–derived lymphocytes (B-lymphocytes), which are responsible for antibody production, are also relatively spared.

Laboratory abnormalities characteristic of AIDS include lymphopenia, specifically a decrease in the T-helper lymphocytes resulting in a reversal in the ratio of T-helper cells to T-suppressor cells. Lymphocyte function is also abnormal.

Since HIV predominantly, although not exclusively, attacks lymphocytes, the greatest concentration of the virus has been isolated from blood, semen, and vaginal secretions. However, it has also been found in human milk, spinal fluid, saliva, and tears.[30, 42]

Definition

The Centers for Disease Control (CDC) revised the case definition for AIDS in adults in 1987.[12] AIDS patients are those HIV-infected individuals with one of several specific opportunistic infections, neoplasias, dementia, or wasting syndrome. The diagnosis of AIDS can be made in the absence of laboratory evidence of infection if the individual has no known explanation of immune deficiency and has one of a number of indicator diseases (for example, *Pneumocystis carinii* pneumonia). The term ARC (AIDS-related complex) is no longer used in CDC classifications. These were patients with HIV infection who were symptomatic but did not fulfill AIDS criteria.

The CDC has developed a classification system based on clinical findings present in the patients.[10] Patients with group I disease have acute infection, group II are asymptomatic carriers, group III have lymphadenopathy, and group IV have symptomatic disease and constitutional symptoms (AIDS). This system is useful in disease reporting and surveillance in public health departments.

In 1987, the CDC also published a classification system for HIV infection in children younger than 13 years of age.[10] The surveillance definition of infection in infants younger than 15 months of age requires the presence of virus in blood (or other tissues) or the presence of antibody with evidence of both cellular and humoral immune deficiency and that certain clinical criteria also be present. Thus, infants who are seropositive but asymptomatic are classified as having "indeterminate infection."

Diagnostic Tests

Tests for IgG antibody for HIV are readily available in most hospitals. The enzyme-linked immunosorbent assay (ELISA) method is used first as a screening test and repeated if positive. If the repeat test is also positive, then a confirmatory test such as the Western Blot must be performed prior to reporting the result to the patient. False-positive results are more likely to occur with the screening ELISA method (particularly if the patient is not in a high-risk group for HIV infection). Reliable HIV-specific tests for IgM antibody and HIV serum antigen have not yet been developed at this time.

HIV can be isolated from blood, other body fluids, and tissues, but this technique is impractical for widespread screening because a culture for HIV can take up to 4 weeks to complete.

Natural History

In adults, infection begins with exposure to HIV by blood, semen, or vaginal secretions (usually through sexual contact). Seroconversion develops within 2 to 16 weeks, but this latent period or "window" may infrequently be much longer.[32]

After initial infection, some individuals experience a mild viral-like or transient febrile illness, subsequently becoming asymptomatic for a highly variable length (months to many years). Even though asymptomatic, most infected individuals will eventually show evidence of laboratory immune dysfunction, which may herald the onset of nonspecific symptoms or conditions (for example, weight loss, fever, lymphadenopathy, candidal infections). These disorders usually are progressive and precede the development of an indicator disease diagnostic of AIDS (for example, Kaposi's sarcoma, *Pneumocystis carinii* pneumonia).

The most complete data for progression of this disease has been obtained from homosexual and bisexual men.[35] No such studies are available yet in women. Based on this data, however, 20% of HIV-infected persons were diagnosed as having AIDS within 5 years of seroconversion. By 6 years after infection, 25% of patients have developed AIDS. The risk of disease progression may not be the same for other risk groups such as hemophiliacs. Because this disease was first noted in 1981, longitudinal observations regarding the long-term risk of HIV-infected individuals developing AIDS are limited.

Once the diagnosis of AIDS is made, the prognosis is dismal. The cumulative probability of survival has been estimated at 49% at 1 year after diagnosis and only 15% after 5 years.[35] As of August 31, 1989, there were 102,621 reported cases of AIDS in the United States and 58,447 deaths.[8] It is anticipated that by 1991 there will be a cumulative total of 270,000 cases of AIDS, with 179,000 deaths.[31]

WOMEN INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS

Overview

Most women contract HIV by the use of intravenous drugs (51%) or sexual relations with IV drug users.[2] As one might expect, the incidence of women with AIDS is highest in those communities in which IV drug abuse is prevalent. Eighty per cent of the women are black or Hispanic, and most of the cases have occurred in New York, New Jersey, Florida, and California. However, HIV infection and AIDS have been reported from almost all states in the country. Alarmingly, recent data suggest that heterosexual activity is becoming an increasingly important role in transmission of this virus. For women, this mode of transmission has increased over the last several years from 12 to 28%.[2] Almost half of HIV-infected women acknowledge no risk behavior.[26] Screening surveys of U.S. Army recruits indicate a 0.6 per 1000 frequency of HIV infection in women.[7] If this rate is similar among child-bearing women, it can be estimated that several thousand HIV-infected pregnancies presently occur in the United States annually.

WOMEN AT RISK FOR HUMAN IMMUNODEFICIENCY VIRUS INFECTION

Obstetric care providers must actively seek out women at risk for HIV infection because few women will request testing or voluntarily provide the information about risk behaviors. Types of experiences that increase a woman's chances of being infected with HIV include current or prior use of illicit IV drugs, receiving blood transfusions or other blood products before 1985, undergoing artificial insemination with donor semen (especially if frozen semen is not used), engaging in prostitution, and having a history of sexually transmitted ulcerative diseases such as herpes simplex infection or syphilis. Other important risk groups include women having sexual contact with (1) someone who has AIDS or has tested positive for HIV, (2) someone who is at risk of infection through sexual practices, and (3) someone who uses IV drugs. Women who come from countries where heterosexual transmission is thought to be the major mode of transmission (for example, Haiti and Central Africa) and women from an area of known or suspected high HIV prevalence (for example, Newark or New York City) should also be considered at risk.

Testing for HIV antibody (after counseling and informed consent) should be offered to women in risk groups who are pregnant or contemplating pregnancy. If there is no antibody to HIV or clinical evidence of HIV disease, these women should be offered counseling about prevention of infection. To reduce the risk of HIV infection, IV drug abusers should be asked to stop using drugs and discouraged from sharing needles and syringes. Women should be informed about safer sexual practices including the use of condoms and a spermicide containing nonoxynol-9. Sexual behavior that can tear or break the skin and body tissues should be avoided. Women who continue high-risk behavior should have their HIV-antibody test repeated periodically during pregnancy to identify seroconversion. They should be counseled not to donate blood or organs. Infants of at-risk women should be evaluated and watched closely for possible HIV infection.

Failure to identify women in these risk groups and provide them with appropriate counseling and testing for HIV infection may have numerous medical as well as legal implications for the health care provider.

HUMAN IMMUNODEFICIENCY VIRUS INFECTION DURING PREGNANCY

Effects of Pregnancy on Human-Immunodeficiency-Virus–Related Disease

Several retrospective studies have raised concerns that pregnancy may enhance the progression of HIV-related disease.[28, 29, 39] These uncontrolled studies suggested that 45 to 75% of infected pregnant women progress from an asymptomatic state to overt clinical disease within 2½ years of delivery. This rate is substantially higher than the rates generally quoted for HIV-infected homosexuals, IV drug users, and adult hemophiliacs. Overall, 10 to 20% of HIV-infected adults develop AIDS within 5 years.[1] The women in these studies were identified only after their children developed AIDS and thus may represent a subgroup with increased risk of disease progression. The progression rate in nonpregnant HIV-infected women is unknown. Furthermore, a recent prospective study of HIV-infected pregnant IV drug users failed to demonstrate a clearcut acceleration in HIV-disease status during pregnancy or the first 28 months of postpartum follow-up.[40]

Recently, in a retrospective study on pregnancy-associated deaths due to AIDS in the United States, Koonin et al[24] reported that the mean interval between diagnosis of AIDS and death was 113 days. The mean length of survival between the diagnosis of AIDS and death in women has been previously reported as 298 days.[35] The difference in mean survival intervals of these two groups tends to support the concern that pregnancy may adversely influence the course of HIV infection. Most of the women in this report were IV drug users or the partner of an IV drug user (75%), and most died of *Pneumocystis carinii* pneumonia.

Evidence that pregnancy clearly alters host immunity, along with reports of increased maternal morbidity and mortality with oral viral illnesses, still raises questions about the safety or pregnancy for the HIV-infected woman. Nonspecific symptoms commonly associated with pregnancy may mask early symptomatology of HIV-related disease and thus delay the diagnosis of AIDS and potentially delay or modify appropriate treatment. The long-term effect of pregnancy on maternal HIV disease is unclear at present based on currently available information.

The Effect of Human Immunodeficiency Virus Disease on Pregnancy

Retrospective studies have suggested that the seropositive woman and her exposed infant may be at an increased risk of adverse pregnancy outcomes.[29, 39] These complications include preterm delivery, intrauterine growth retardation, stillbirth, spontaneous abortion, and low birthweight neonates. Many of these complications may be attributable to the high prevalence of IV drug use and low socioeconomic status in this group of women.

Selwyn et al,[40] in a prospective study evaluating pregnancy outcomes of seropositive IV drug users with matched seronegative IV drug user controls, found no differences in the frequency of spontaneous abortion, ectopic pregnancy, preterm delivery, stillbirth, or low birthweight neonates. However, substantially more seropositive than nonseropositive gravida (24 versus 5%) were hospitalized for serious non-AIDS-defining infectious diseases (that is, bacterial pneumonia) during pregnancy.

A major concern for the HIV-infected gravida, as well as her care provider, is the rate of perinatal transmission of the virus to the fetus or neonate. Initial studies reported rates as high as 50 to 65%.[28, 29, 39] However, these studies focused on rates in children of mothers who had already delivered infected children and probably represent a different subset of women who are at increased risk of transmitting the virus perinatally.

Recent prospective studies report a 20 to 40% transmission rate.[6, 25, 34, 36] These studies are hampered by the persistence of passively acquired maternal antibody in the neonate for up to 15 months.

Interpretation of the current data, especially when used to counsel infected gravida, must be done with caution.

Antepartum Care

In the first or early second trimester, pregnancy termination is an option that should be discussed with the known seropositive patient. For the woman continuing her pregnancy, certain modifications in prenatal care need to be made.

In addition to the routine prenatal screening tests for gonorrhea and syphilis, it is wise to test for other sexually transmitted diseases such as *Chlamydia* and hepatitis B. The immune-impaired HIV-infected patient is also at greater risk for *Mycobacterium tuberculosis*, toxoplasmosis, and cytomegalovirus (CMV) infection. Tuberculosis skin testing should be performed. Baseline antibody titers for toxoplasmosis and CMV are recommended, as primary infection during pregnancy with these agents may have grave consequences for the fetus. Repeat titers can be drawn later if symptoms subsequently occur.

Measuring T-cell values in asymptomatic HIV-positive women may help identify those at greater risk for developing serious infectious complications during their pregnancy.[25] T-cell levels in HIV-infected and uninfected women drop during pregnancy and reach a nadir of 700 to 800 T_4 cells per μL.[25] Most HIV-positive pregnant women have T-cell values close to the normal range (10 to 20% lower than seronegative controls). Pregnant women with values of fewer than 300 T_4 cells per μL are uncommon and may develop serious pregnancy complications.[25, 36] Infected women with less than 400 T_4 cells per μL may have a greater chance of transmitting the virus to their infants.[36]

Clinicians should be suspicious of nonspecific complaints such as fatigue and weight loss. Common opportunistic infections such as *Pneumocystis carinii* pneumonia, severe herpes simplex episodes, and oropharyngeal candidiasis do not pose a direct threat to the fetus but may cause serious maternal illness. Although certain antiviral or antibacterial drugs could have theoretical effects on fetal development, current standard or recommended therapeutic regimens should not be withheld from the mother.

Currently, azidothymidine (AZT) has been the only approved antiretroviral agent used to combat the AIDS virus. The safety of AZT in pregnancy has not been established. The efficacy of AZT in preventing transplacental or neonatal transmission of the virus is also unclear. However, protocols are currently under investigation by the Pediatric Committee for AIDS Cooperative Group of the National Institute of Allergy and Infectious Disease.

The obstetric care provider should be familiar with common and uncommon manifestations of HIV infections and their treatments, but when faced with severe HIV-related disease, knowledgeable physicians with expertise in the field of AIDS should be called upon.

Intrapartum Care

Delivery method does not appear to change the risk of perinatal transmission of HIV. Minkoff et al[28] reported that a third of 34 HIV-infected infants in this study had been delivered by cesarean section. HIV has also been isolated from a full-term placenta, suggesting that this virus crosses the placenta hematogenously and that cesarean section will have little benefit or role in preventing perinatal transmission.[20]

However, since the exact time of perinatal transmission of HIV has not been identified, it seems prudent to limit other potential sources of intrapartum transmission. Evaluation of fetal status by fetal scalp blood sampling or application of an internal scalp electrode seems best avoided when possible. Theoretically, these procedures may enhance innoculation of the virus into the fetus.

Hematologic changes sometimes seen in HIV-positive patients include thrombocytopenia, anemia, mild increases in the bleeding time, abnormal clot formation, and platelet aggregation. The potential for increased bleeding in these patients should be kept in mind when operative delivery is considered or when obstetric conditions exist that would predispose the patient to hemorrhagic complications (that is, preeclampsia or placenta previa).

Effects of Surgery and Anesthesia on Human-Immunodeficiency-Virus–Related Disease

Anecdotal reports have appeared in the literature expressing concern that HIV-related disease may be accelerated by surgical procedures and anesthesia. Yet there are no scientific data to support or refute these contentions. Scannell[37] recently reviewed the available studies published in the literature that have investigated the immunomodulating effects of surgery and anesthesia in people without HIV-related disease. The effects seen are generally those of immune suppression and often depend on the type of anesthesia used and the extent of surgery performed. However, these alterations appear to be transient and rarely correlated with adverse clinical outcomes.

Changes in cellular immunity associated with surgery and anesthesia may include depressions of natural killer cell (NKC) activity and numbers, lymphocyte proliferation and blastogenic responses, delayed type hypersensitivity, B-cell function, and granulocyte function.

NKC (a subpopulation of lymphocytes thought to play a role in the body's defense against certain microbial infections) activity and numbers appear to be depressed for 3 to 6 days after major surgery but not minor surgical procedures. Postoperative NKC activity is also influenced by the mode of anesthesia. NKC activity is unchanged postoperatively after spinal or extradural anesthesia, although it may decrease after general neuroleptic anesthesia. This differential effect on the immune system has been shown in studies of women undergoing hysterectomy, elective cesarean sections, and minor gynecologic procedures.[37] In no instance did these changes correlate with clinical outcome although, theoretically, the potential consequences of this impaired cell-mediated immunity would include a greater chance of postoperative sepsis, infection, colonization of tissues and wounds, and poor wound healing.

People infected with HIV may demonstrate the same laboratory abnormalities of immunologic testing that are transiently seen in noninfected individuals undergoing surgical interventions. Concern that anesthesia and surgery could further impair their immune status, placing them at greater risk for postoperative complications or enhancement of other HIV-related disease, seems reasonable. This is speculative, however, and the few clinical studies of surgical interventions performed in AIDS patients do not demonstrate adverse outcomes attributable to surgery or anesthesia alone.[37]

Concern has been raised that spinal or epidural anesthesia may exacerbate the central nervous system manifestations or other neurologic conditions associated with AIDS.[18] However, this theoretical fear is not substantiated by any reported cases in which spinal or epidural anesthesia was thought responsible for initiating or worsening the neurologic condition of an AIDS patient. On the contrary, it appears that spinal or epidural anesthesia, which has been shown to cause less immunologic disturbances than general anesthesia, may be the more prudent anesthetic choice for the HIV-infected individual. Finally, because tracheal intubation may increase the risk of upper respiratory colonization and aspiration, general anesthesia seems best avoided in the AIDS patient whenever possible.

Thus, for the HIV-infected gravida, the decided route of delivery and mode of anesthesia should be based on the usual obstetric considerations only.

Postpartum Care

Breastfeeding has been implicated as a possible mode of transmission of the virus from the mother to the infant and is not recommended for HIV-seropositive women.[4] The HIV-positive mother should otherwise be allowed full access to her infant.

Although the immediate postpartum course of these women does not appear to be unduly complicated, postpartum endometritis should be aggressively and promptly treated. The patient should be referred to a physician or center with expertise in treating HIV-related disease for ongoing medical care.

HUMAN IMMUNODEFICIENCY VIRUS INFECTION CONTROL IN THE OBSTETRIC SETTING

Information obtained from all persons with AIDS reported to the CDC includes a question about employment in a health care or clinical laboratory setting. Current reviews of surveillance data support other studies indicating that the risk of HIV transmission in the occupational setting remains low and is most often associated with percutaneous innoculation of blood from a patient with HIV infection.[13, 27] The risk of seroconversion after inadvertent HIV exposure during needlestick injury is less than 0.5%.[13] To date, no cases of occupational transmission of HIV to labor and delivery room personnel have been recorded. However, office and hospital infection control procedures should be uniform for all patients.

The CDC has published detailed guidelines to help prevent the transmission of HIV and other blood-borne pathogens.[11, 14] These include the use of gloves for all procedures in which secretion contact is possible; handling of all patient specimens as if they were infectious; avoidance of needle resheathing and disposing of them in puncture-resistant containers; and cleaning contaminated surfaces or sterilization of reuseable items according to standard protocols.

Other specific infection control measures during delivery include the use of gloves at all times, the use of water-resistant gowns, and the wearing of masks and protective eye covering. Gloves should always be worn while handling the neonate until after its first bath when maternal secretions will no longer be present. The placenta should be considered infectious and handled or examined with gloves. Another unique obstetric concern involves the avoidance of oral suction devices (DeLee suction devices) for neonatal airway suction. Wall suction or bulb suction should be used exclusively. With devices that operate by mouth suction, a trap should be placed in the line.

These precautions should not be limited to those patients known to be HIV-antibody positive, because the clinician is probably most at risk from unidentified infected patients who are not appropriately managed.

THE ECONOMIC CONCERNS OF PERINATAL AIDS

Although children now represent a small proportion (1 to 2%) of all patients with AIDS, the total number of pediatric cases reported has risen from 64 in December 1983 to 1736 in August 1989.[8] It is estimated that as many as 10,000 to 20,000 children may be diagnosed with AIDS by 1991. Over 80% of these children will have contracted the virus from their mother.

Hegarty et al[19] reported that the total cost of hospital care for HIV-infected children at Harlem Hospital Center between 1981 and 1986 was $3.3 million. Average lifetime costs were $90,347 per child, more than three times the cost for an adult homosexual male in San Francisco with the disease.[38] The mean length of stay for children who died was 129 days. The accumulative mean lifetime hospitalization of an adult with AIDS in San Francisco was 35 days. Studies that have addressed the cost of caring for IV drug-using patients with AIDS are not available.

One third of total inpatient days and over 20% of the cost of hospital care for infected children result from social factors and are not medically necessary.[19, 23] Many "boarder babies," HIV-seropositive children who are healthy enough to go home, remain in the hospital awaiting difficult-to-find foster home placement after their parents died, abandoned them, or proved unable to care for them.

But even excluding days of care that were not medically necessary, HIV children required on average 63% more days in the hospital per year than the average adult AIDS patient, reflecting the greater severity of AIDS in children.[22, 33, 35] Pediatric HIV disease differs from the adult disease in several important ways. The incubation period is shorter, the cumulative mortality rate is higher, and infected children are particularly predisposed to recurrent episodes of severe bacterial infections.

A report by Andrulis et al[3] clearly demonstrates that public hospitals and private teaching hospitals have cared for a disproportionate number of patients with AIDS. The distribution by payor source is striking—54% Medicaid and only 17% private insurance. Furthermore, 97% of the children in Hegarty's study were Medicaid-eligible, and only 3% had private insurance. The average costs per day for patients with AIDS far outdistance revenue generated per day in institutions where Medicaid represents the most frequent third-party payor.[3, 4] The escalating costs of treating HIV-related disease will profoundly affect certain major public and private teaching institutions in the near future. The adverse impact this may have on our ability to provide optimal care to all patients cannot be overemphasized.

HUMAN IMMUNODEFICIENCY VIRUS INFECTION: LEGAL CONCERNS

Few physicians have spent much time worrying about the legal risks of caring for women with AIDS or HIV infection. A whole new specialty, AIDS law, is creating new possibilities for legal actions.[5]

Historically, all deadly communicable diseases have triggered fear, hysteria, and prejudice against the afflicted. A similar uneasiness about treating HIV-infected patients exists today among the medical community. This is especially true for those who perform procedures that greatly increase the risk of exposure to patients' blood and bodily fluids (surgeons, emergency room personnel, and trauma specialists). Past Surgeon General C. Everett Koop told the President's Commission on AIDS that physicians have a duty to treat all patients, regardless of their disease, with one exception. Surgeons, with greater risk by virtue of greater-than-normal exposure to blood, would have to make their own decisions in cases regarding AIDS.[5] The American College of Surgeons has adopted the Surgeon General's position; however, the American Medical Association and the American College of Obstetricians and Gynecologists have stated that all physicians have an ethical obligation to care for AIDS patients.

Almost all state medical examining boards have developed policies on the physician's duty to provide care for AIDS patients. "Patient abandonment" and "failure to treat" may risk not only the physician's loss of license but are also two of the most difficult malpractice charges to defend.[5]

Failure to diagnose and institute treatment in a timely fashion are two common reasons for malpractice actions. Since "normal" nonspecific pregnancy symptoms can mimic other diseases, failure to diagnose AIDS in pregnancy may easily become a reason for malpractice suits in obstetrics. Since infected gravida can transmit HIV to their infants, children of infected women who contract the disease may also have actions brought on their behalf. Two malpractice dangers, "failure to inform" and "duty to warn," open the door to potential litigation. For instance, a wrongful birth suit could result if a pregnant woman at risk for HIV infection is not offered testing for the virus or counseled about the significance of the test results. A malpractice suit is also possible if an HIV test is obtained without informed consent, especially if results are used in a harmful or discriminatory way. Physician-patient confidentiality in AIDS cases may be in direct legal opposition to the duty to warn endangered third parties (spouses and medical staff). The tendency is to assume that, if the need to warn is urgent enough, a breech of confidentiality is warranted.

Most states have passed, or are considering, specific statutes regarding these issues. State health departments have issued recommendations to govern HIV-testing policies and reporting of HIV-positive cases in lieu of specific legislation. The obstetric health provider is urged to learn what policies or laws have been established regarding HIV testing in his or her own state.

SUMMARY

Since neither a vaccine nor a safe, effective drug against the AIDS virus exists, health care providers will increasingly be faced with HIV-related problems. It appears that pregnancy adversely impacts on HIV-related disease and that the opposite is also true. Conflicting data now exist that emphasize more prospective studies are needed before we will have definitive answers.

Prevention of new HIV infections is currently the only means we have to slow this epidemic. Health care providers must redouble their efforts to educate, counsel, and offer testing to at-risk women. Preventing transmission of the virus during pregnancy, parturition, and the neonatal period offers the greatest hope of ameliorating pediatric AIDS. Studies of therapeutic or prophylactic interventions during the perinatal period, whether pharmacologic or immunologic, to combat HIV infection should be of high priority.

The toll-free number to receive updated AIDS information from the CDC is 1-800-342-2437; information for health care providers can also be obtained. The Burroughs Wellcome Pharmaceutical Company has initiated a study to determine the effectiveness of zidovudine (Retrovir, AZT) in preventing the establishment of HIV infection in health care workers occupationally exposed to HIV.

REFERENCES

1. ACOG: Human immune deficiency virus infections. ACOG Technic Bull 128:1, 1988
2. ACOG: Prevention of human immune deficiency virus infection and acquired immune deficiency syndrome. ACOG Committee Statement 1, 1987
3. Andrulis DP, Beers VS, Bentley JD, et al: The provision and financing of medical care for AIDS patients in U.S. public and private teaching hospitals. JAMA 258:1343, 1987
4. Arno PS: The economic impact of AIDS. JAMA 258:1376, 1987
5. Ballad R: Avoiding malpractice in AIDS cases. Contemp Obstet Gynecol 33:178, 1989
6. Blanche S, Rouzioux C, Guihard ML, et al: A prospective study of infants born to women seropositive for human immunodeficiency virus type I. N Engl J Med 320:1643, 1989
7. Burke DS, Brundage JF, Herbold JR, et al: Human immunodeficiency virus infections among civilian applicants for United States military service, October 1985 to March 1986. Demographic factors associated with seropositivity. N Engl J Med 317:131, 1987
8. Centers for Disease Control: AIDS weekly surveillance report, United States, August 31, 1989
9. Centers for Disease Control: CDC classification system for human T-lymphotropic virus type III/lymphadenopathy associated virus infections. MMWR 35:334, 1986
10. Centers for Disease Control: Classification system for HIV infection in children under 13 years of age. MMWR 36:225, 1987
11. Centers for Disease Control: Recommendations for prevention of HIV transmission in health-care settings. MMWR 36:35, 1987
12. Centers for Disease Control: Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. MMWR 36:35, 1987
13. Centers for Disease Control: Update: Human immunodeficiency virus infections in health-care workers exposed to blood of infected patients. MMWR 36:285, 1987
14. Centers for Disease Control: Update: Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus and other bloodborne pathogens in health-care settings. MMWR 37:377, 1988
15. Feinkind L, Minkoff HL: HIV in pregnancy. Clin Perinatol 15:189, 1988
16. Francis DP, Chin J: The prevention of acquired immunodeficiency syndrome in the United States. JAMA 257:1357, 1987
17. Gallo RC, Salahuddin SZ, Poporic M, et al: Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS. Science 225:500, 1984
18. Greene ER: Spinal and epidural anesthesia in patients with the acquired immunodeficiency syndrome. Anesth Analg 65:1090, 1986
19. Hegarty JD, Abrams EJ, Hutchinson VE, et al: The medical care costs of human immunodeficiency virus—infected children in Harlem. JAMA 260:1901, 1988
20. Hill WC, Bolton V, Carlson JR: Isolation of acquired immunodeficiency syndrome virus from the placenta. Am J Obstet Gynecol 157:10, 1987
21. Holman S, Berthaud M, Sunderland A, et al: Women infected with human immunodeficiency virus: Counseling and testing during pregnancy. Semin Perinatol 13:7, 1989
22. Katz BZ: Natural history and clinical management of the infant born to a mother infected with human immunodeficiency virus. Semin Perinatol 13:27, 1989

23. Kemper K, Forsyth B: Medically unnecessary hospital use in children seropositive for human immunodeficiency virus. JAMA 260:1906, 1988
24. Koonin LM, Ellerbrock TV, Atrash HK, et al: Pregnancy-associated deaths due to AIDS in the United States. JAMA 261:1306, 1989
25. Landesman SH: Human immunodeficiency virus infection in women: An overview. Semin Perinatol 13:2, 1989
26. Landesman SH, Minkoff HL, Holman S, et al: Serosurvey of human immunodeficiency virus infections in parturients: Implications for human immunodeficiency virus testing programs of pregnancy women. JAMA 288:2701, 1987
27. Lifson AR, Castro KG, McCray E, et al: National surveillance of AIDS in health care workers. JAMA 256:3231, 1986
28. Minkoff H, Nanda D, Menez R, et al: Pregnancies resulting in infants with acquired immunodeficiency syndrome or AIDS-related complex. Obstet Gynecol 69:285, 1987
29. Minkoff H, Nanda D, Menez R, et al: Pregnancies resulting in infants with acquired immunodeficiency syndrome or AIDS-related complex: Followup of mothers, children and subsequently born siblings. Obstet Gynecol 69:288, 1987
30. Peterman TA, Curren JW: Sexual transmission of human immunodeficiency virus. JAMA 256:2222, 1986
31. Public Health Service: Coolfont Report: A PHS Plan for Prevention and Control of AIDS and the AIDS Virus. Public Health Rep 101:341, 1986
32. Rank A, Krohn M, Allain JP, et al: Long latency precedes over seroconversion in sexually transmitted human immunodeficiency virus infection. Lancet 2:589, 1987
33. Rogers MF: AIDS in children: A review of the clinical, epidemiologic and public health aspects. Pediatr Infect Dis J 4:230, 1985
34. Rogers MF, Ou CY, Rayfield M, et al: Use of the polymerase chain reaction for early detection of the proviral sequences of human immunodeficiency virus in infants born to seropositive mothers. N Engl J Med 320:1649, 1989
35. Rothenberg R, Woelfel M, Stoneburner R, et al: Survival with acquired immunodeficiency syndrome. N Engl J Med 317:1297, 1987
36. Ryder RW, Nsa W, Hassig SE, et al: Perinatal transmission of the human immunodeficiency virus type I to infants of seropositive women in Zaire. N Engl J Med 320:1637, 1989
37. Scannell KA: Surgery and human immunodeficiency virus disease. AIDS 2:45, 1989
38. Scitorsky AA, Cline M, Lee PR: Medical care costs of patients with AIDS in San Francisco. JAMA 256:3103
39. Scott GB, Fischl MA, Klinas N, et al: Mothers of infants with the acquired immunodeficiency syndrome. Evidence for both symptomatic and asymptomatic carriers. JAMA 253:363, 1985
40. Selwyn PA, Schoenbaum EE, Daveny K, et al: Prospective study of human immunodeficiency virus infection and pregnancy outcomes in intravenous drug users. JAMA 261:1289, 1989
41. Sever JL, Larsen JW, Grossman JH: Handbook of Perinatal Infections, ed. 2. Boston, Little Brown, 1989, p 22
42. Ziegler JB, Cooper DA, Johnson RO, et al: Postnatal transmission of AIDS associated retrovirus from mother to infant. Lancet 1:896, 1985

Address reprint requests to

Cathy Jo Cantrell, MD
Department of Reproductive Medicine
University of California, San Diego
402 Dickinson Street
San Diego, CA 92103

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Critical Care for the Pregnant Patient

*Ronald Dworkin, MD,**
and Thomas G. Karagianes, MD†

The critical care management of the pregnant patient requires an application of conventional intensive therapy to a patient whose physiology is quite different from the nonpregnant state. Although the literature reports some experience in how to manage pregnant patients in the intensive care unit (ICU), many recommendations must originate by merging the purposes of intensive therapy with a knowledge of the physiology of pregnancy. Furthermore, the management of the obstetric patient must take into account the need to prevent preterm labor and fetal well-being. The article discusses selected aspects of critical care medicine applied to obstetric patients with particular emphasis on cardiopulmonary physiology and management, hemodynamic monitoring, and mechanical ventilation.

CARDIOVASCULAR CONSIDERATIONS

The pregnant patient is at risk for hypotension secondary to decreased cardiac preload primarily as a result of aortocaval compression.[28] Beginning as early as 20 weeks gestation, the gravid uterus can obstruct the inferior vena cava in the supine patient, leading to a decrease in venous return. For this reason, the pregnant patient should not be kept flat on her back in the ICU. If hypotension does occur, aortocaval compression must be relieved by left (or occasionally right) uterine displacement. Trendelenburg's position without left uterine displacement is not sufficient. The "supine hypotension syndrome" must be added to the differential diagnosis of hypotension in the pregnant ICU patient as a primary diagnosis or as an exacerbating factor.

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* Staff, Department of Anesthesiology, Greater Baltimore Medical Center, Baltimore, Maryland

† Assistant Clinical Professor, Department of Anesthesiology, University of California, San Diego School of Medicine; Associate Director, Surgical Intensive Care Unit, University of California, San Diego Medical Center, San Diego, California

The hypotension secondary to aortocaval compression or any cause is detrimental to both mother and fetus. Because the uterine blood vessels are presumed to be maximally dilated, uteroplacental blood flow is relatively perfusion pressure dependent. Hypotension must be corrected rapidly for a systolic blood pressure (SBP) of less than 70 mm Hg and aggressively for a SBP of less than 90 to 100 mm Hg to ensure adequate uteroplacental flow.

The initial treatment of modest hypotension in the pregnant patient includes left uterine displacement and intravascular volume infusion. Synthetic noncatecholamines can be used as temporizing measures to raise blood pressure until further evaluation and additional treatment can be instituted. Ephedrine and mephenteramine are preferred (rather than metaraminol or phenylephrine) because they result in a greater improvement in uteroplacental blood flow when correcting hypotension.[18]

As a corollary to the need to rapidly correct hypotension in the pregnant patient is the issue of acceptable blood pressure during induced hypotension. The adequacy of uterine perfusion will dictate the extent to which the maternal blood pressure can be lowered therapeutically. Patients with certain vascular lesions (for example, intracranial aneurysm) require hypotension to decrease the stress on the fragile vessel wall. Although a mean blood pressure of 50 mm Hg may be the point at which cerebral autoregulation is exhausted and cerebral blood flow beings to decrease, a higher blood pressure is probably required to maintain uteroplacental flow. It seems appropriate to use a SBP of 90 to 100 mm Hg as a safe end point when reducing maternal blood pressure. The duration of the hypotensive therapy can also impact fetal risk; therefore, the prolonged use of deliberate hypotension or afterload reduction in the pregnant patient requires special consideration. Continuous fetal heart rate monitoring should be used in the ICU to help evaluate the effects of therapy on the fetus after the 18th week of gestation, as is done in the operating room.

Assuming uterine venous pressure exceeds intrauterine pressure, uterine blood flow (UBF) is determined by the equation:

$$\mathrm{UBF} = \mathrm{UAP} - \mathrm{UVP}/\mathrm{UVR}$$

where UAP = uterine arterial pressure; UVP = uterine venous pressure; and UVR = uterine vascular resistance. It follows that factors other than maternal blood pressure determine the adequacy of uteroplacental flow. Increases in UVR secondary to maternal disease or to physiologic manipulations may lead to higher blood pressure requirements. Both hypocarbia secondary to mechanical ventilation[12] and vasopressors can increase UVR.[22] An increased UVP secondary to elevated right atrial pressure from disease (for example, right ventricular failure) or therapy (for example, PEEP) may also lead to higher blood pressure requirements.[11]

Hypotension in the pregnant patient may be secondary to inadequate cardiac contractility, and inotropic therapy may be required.

Recommendations for inotropic agents in the pregnant patient are not well established. Dopamine in animals has been reported to both increase and decrease uterine blood flow. The decrease may be secondary to the α-agonist effects that result when the dose is raised above 10 μg per kg per minute.[3, 22] The effects of dobutamine, which lacks α-agonist properties, have not been carefully examined in the pregnant patient. Epinephrine can increase maternal blood pressure, while markedly decreasing uterine blood flow.[9] Furthermore, its β-agonist effects can decrease uterine contractility. In sum, maternal needs will probably dictate the choice of drug when cardiac dysfunction is severe enough to require inotropic support, but the drugs should be used with a degree of caution because of the possible untoward effects on uteroplacental perfusion.

The pregnant patient normally experiences an increase in intravascular volume that begins in the first trimester. This presumably leads to an increase in cardiac preload, although this has not been documented. Plasma volume expansion leads to a 35 to 40% increase in blood volume by term.[28] During labor, uterine contractions add another 300 to 500 mL to the central vascular compartment. Intravascular volume increases further after delivery with the autotransfusion produced by uterine involution.

This "hypervolemic" state can complicate the management of various conditions seen in the ICU. Permeability pulmonary edema and congestive heart failure are two conditions that require careful management of left ventricular filling pressures. To reduce edema fluid formation, current therapy attempts to maintain cardiac output with lower filling pressures. The expanded blood volume of pregnancy does not necessarily lead to higher filling pressures, as will be discussed. At the same time, any reduction in cardiac performance will produce higher filling pressures secondary to the volume expansion of pregnancy. Obstetric patients may, therefore, require additional pharmacologic efforts (for example, the use of venodilators or diuretics) to reduce preload when it may have been otherwise unnecessary in the nonpregnant patient. If preload reduction is required, nitroglycerin can be used, because it has not been associated with any deleterious effects on the fetus or with a decrease in uterine blood flow independent of its hypotensive effect.[29, 32] Furosemide has not been shown to produce congenital defects in the fetus and can be used in the pregnant patient. However, it does cross the placenta and may cause a diuresis in newborns.

Other vasodilators can be used in the pregnant patient. Clinically significant cyanide levels remain a concern when using nitroprusside, and prolonged administration has been shown to result in fetal death in ewes.[13] Therefore, the drug can only be safely used for short periods of time (for example, 15 minutes), thereby significantly curtailing its utility in the ICU. Hydralazine has often been used to control hypertension in preeclamptic patients, and the drug does not appear to compromise uterine blood flow or fetal safety.[20]

HEMODYNAMIC MONITORING

Placement of Invasive Monitors

The critically ill obstetric patient may require invasive hemodynamic monitoring. There are a number of sites through which to gain access to the central venous circulation. In addition to the advantages and complications of each route, there are some special considerations in the pregnant patient.

The coagulation status of the obstetric patient should be evaluated prior to central venous cannulation. Most pregnant patients have normal clotting function (and are even described as hypercoagulable), but patients with preeclampsia may have a coagulopathy secondary to platelet dysfunction. Patients with placental abruption, retained dead fetus, and amniotic fluid embolism may experience disseminated intravascular coagulation. In these individuals, catheterization might initially be attempted in the basilic vein in the antecubital fossa or in the external jugular vein. At these sites, bleeding can be well controlled and would not be catastrophic.[27]

Subclavian vein catheterization should probably not be performed when a coagulopathy is present to avoid potentially significant hemorrhage if the subclavian artery is punctured.[27] Internal jugular vein catheterization might also be avoided in such patients to avoid the hemorrhage of inadvertent carotid artery puncture, although this site can be more easily compressed than the area adjacent to the subclavian artery. The risk of an enlarging neck hematoma resulting in airway compression is present when internal jugular vein cannulation is attempted.[27]

Rigid guidelines cannot replace clinical judgement, but criteria for avoiding internal jugular and subclavian vein puncture, including a prothrombin time 3 seconds greater than control and a platelet count less than 50,000 plt per μL^3, have been offered.[27] It is important to note, however, that the data regarding acceptable limits are unclear and that many of the bleeding complications from internal jugular vein cannulation have been reported in patients who were subsequently heparinized. In one study of internal jugular vein cannulation in patients with severe coagulopathy secondary to chronic liver disease, only 1 patient out of 1000 experienced a hematoma large enough to cause airway compression.[8]

Femoral vein catheterization is also used in the ICU to avoid the complications of internal jugular or subclavian vein catheterization in patients with a coagulopathy. Thrombosis of the inferior vena cava or the ileofemoral veins is the most feared complication of using this site. The pregnant patient has increased intra-abdominal pressure and may experience frequent transient obstruction of the inferior vena cava secondary to aortocaval compression. This combined with the hypercoagauble state of pregnancy may predispose the pregnant patient to this complication. In the nonobstetric patient, increased intra-abdominal pressure and inferior vena cava obstruction have been described as contraindications to inferior vena cava catheterization. Furthermore, the central venous pressure catheter would have to be advanced to the intrathoracic region, as the increased intra-abdominal pressure of pregnancy would produce falsely elevated central venous pressures. Finally, right lower quadrant bowel perforation has been described as a complication of femoral venipuncture[26] and, in the pregnant patient, uterine puncture might also occur. In sum, femoral vein catheterization should be avoided in the pregnant patient.

Pulmonary artery catheterization is associated with the same complications as in the nonpregnant patient. These include dysrhythmias, bundle branch block, pulmonary artery rupture, pulmonary infarction, catheter-related infections, balloon rupture, and endocardial damage. In a very small study of 21 pregnant patients with severe preeclampsia, the most common complications during catheter insertion included dysrhythmia (two patients), balloon rupture (one patient), and positive culture of the catheter tip without evidence of septicemia (one patient).[16] The authors of this study noted that despite the hypercoagulable state of pregnancy and the common finding of thrombi along the length of the catheter, pulmonary embolization or infarction was not noted.

There are no major obstetric considerations for cannulation of the arterial system. As compression of the aorta by the gravid uterus can decrease blood flow to the lower extremities, blood pressure measurements obtained from femoral or dorsalis pedis artery catheters may be erroneously lower than upper-extremity pressures. Lower-extremity hypotension may direct inappropriate intervention if the perfusion pressure of the heart and brain is inferred from blood pressure measured in the lower extremity. Perfusion pressure to these vital organs would be more accurately inferred from an upper-extremity arterial catheter. At the same time, blood pressure measurement in the lower extremities can help detect decreases in uterine arterial blood pressure secondary to uterine compression of the aorta, and prompt the necessary postural changes required to increase uterine artery (and lower-extremity) blood pressure.

Interpretation of Hemodynamic Data

Clinical decisions based on interpretation of hemodynamic data are influenced by knowledge of the normal range of values in pregnancy. There is actually disagreement over what constitutes "normal" in the pregnant patient. Early studies reported a decrease in right atrial pressure (RAP), right ventricular end-diastolic pressure (RVEDP), and mean pulmonary artery pressure (PAP) and a decrease in central blood volume in the normal pregnant patient.[1] However, the results may have been affected by uterine compression of the inferior vena cava that was not corrected. Later studies demonstrated an increase in RAP, RVEDP, PAP, and central blood volume beginning early in pregnancy. Others have cited no change in RAP with pregnancy.

In a recent examination of the hemodynamic effects of oxytocin in women during the first trimester of pregnancy, nine healthy subjects were noted to have a pulmonary capillary wedge pressure (PCWP) of 5 to 10 mm Hg, a PAP of 9 to 14 mm Hg, a pulmonary vascular resistance (PVR) of 35 to 90 dyne per second per cm^5, and a stroke volume of 50 to 75 mL per beat, prior to injection of oxytocin.[24] The patients were anesthetized and mechanically ventilated, which could have perturbed the data relative to the nonanesthetized, spontaneously breathing state. Still, these values would be considered normal for anesthetized, mechanically ventilated nonobstetric patients.

In another study that produced hemodynamic data prior to drug infusion in healthy women during the first trimester of pregnancy, the subjects examined had a central venous pressure from 3 to 5 mm Hg, a PCWP from 4 to 6 mm Hg, a PAP from 14 to 19 mm Hg, and a stroke volume of 50 to 60 mL per beat.[25] These patients were in a sitting position when the data were obtained, which could have affected the values relative to those that might have been obtained in the supine position. Yet, they are similar to values that constitute normal in healthy nonobstetric subjects.

In a third study of hemodynamics, measurements were obtained before and after induction of anesthesia and removal of molar pregnancy during the first trimester.[5] Prior to induction, baseline values included a central venous pressure of 6 mm Hg, a PAP of 14 mm Hg, a PCWP of 10 mm Hg, a PVR of 48 dyne per second per cm^5, a stroke volume of 83 mL per beat, and a systemic vascular resistance (SVR) of 1060 dyne per second per cm^5. Again, these data are similar to those often obtained from normal nonobstetric patients, except for a slightly wider difference between the central venous pressure and the PCWP.

Studies in the obstetric literature have purported a different hemodynamic baseline in preeclamptic patients. In one study of severe preeclamptic patients in early labor receiving a $MgSO_4$ infusion, the authors demonstrated an increase in cardiac output, secondary to an increase in stroke volume and heart rate, compared with normotensive patients in early labor.[20] Unfortunately, hemodynamic data for normotensive patients were obtained from earlier work that did not describe the use of left uterine displacement while collecting data.

Preeclamptic patients have also been reported to have hypereffective hearts.[17] For a given PCWP, the cardiac work is greater than in normal patients; hence, a greater level of cardiac contractility. This assumes normal or reduced left ventricular compliance, and that the greater amount of work is not simply the product of greater ventricular volume. This concept was not examined in the study. Unlike the SVR, the PVR was not significantly affected by preeclampsia.

The relationship between CVP and PCWP in patients with severe preeclampsia was also addressed in this study. In six of the nine patients studied, there was good correlation between CVP and PCWP. In three patients, the CVP did not reflect changes in the PCWP. Unexpectedly and unexplained, the PCWP actually decreased as the CVP increased. This is the opposite of what is commonly seen in patients with left ventricular disease secondary to severe hypertension, in whom volume loading produces a smaller increase in CVP than PCWP.

The CVP-PCWP relationship in severe preeclamptic patients has been explored in another study.[6] Ten of 18 patients had a linear relationship between CVP and PCWP, but interindividual variations prevented accurate prediction of the PCWP from the CVP. In the remaining patients, there was no correlation between CVP and PCWP. It is not known if digital display values were used or if respiratory variation was taken into account, because both can affect the accuracy of the measurements.

In sum, the body of data accumulated from pregnant patients to establish a hemodynamic baseline is not large and is occasionally conflicting, and more studies need to be performed before a thorough understanding can be obtained. However, some tentative conclusions can be drawn from the current data to aid in the management of obstetric patients in the ICU.

The pulmonary vasculature does not appear to be affected by pregnancy, even with preeclampsia. Therefore, increases in PVR are more likely secondary to pulmonary disease and effects of mechanical ventilation and PEEP. Furthermore, the pulmonary artery diastolic pressure is close to the PCWP in the pregnant patient, as when PVR is not elevated.

The central venous pressure in healthy women appears to be unchanged by pregnancy. The previously mentioned studies demonstrate a central venous pressure in women during the first trimester that is similar to that seen in nonpregnant women.

The PCWP appears to be unchanged by normal pregnancy. The PCWP of pregnant patients in the first trimester, and even in many severely preeclamptic patients in the last trimester, is not significantly different from the PCWP observed in healthy nonpregnant patients.

The central venous pressure and PCWP appear to correlate in normal pregnancy, with the central venous pressure offering a reasonable estimate of PCWP in the absence of major physiologic disturbances. Studies of right ventricle and left ventricle compliance would help to determine if a disparity between the central venous pressure and PCWP develops in response to volume loading in certain situations (for example, preeclampsia).

In the preeclamptic patient, the data are less clear. Even in those studies that demonstrated a disparity between central venous pressure and PCWP, many patients with preeclampsia showed a correlation between central venous pressure and PCWP. In those subjects in whom a lack of correlation was demonstrated, the data are somewhat confusing. Therefore, it is difficult to make recommendations regarding invasive monitoring in the preeclamptic patient (that is, whether a central venous pressure or a pulmonary artery catheter is required for management). The decision must combine other elements of concurrent organ dysfunction with clinical experience.

Pregnancy is associated with an increase in stroke volume, as long as venous return is not reduced by inferior vena cava compression.

The etiology of the increase in stroke volume is unclear. It may be secondary to increased left ventricular end-diastolic volume (LVEDV) as a result of the increase in plasma volume. But left ventricular end-diastolic pressure (LVEDP), as approximated by the PCWP and as a measure of LVEDV, does not appear to change significantly in pregnancy. An unchanged LVEDP associated with an increased LVEDV may be due to improved left ventricular compliance during pregnancy. The increased stroke volume may also be due to increased cardiac contractility. The increased stroke volume may also be due to a reduction in afterload that accompanies the decrease in SVR during pregnancy. None of these possibilities have been substantiated because measurement of LVEDV and the assessment of left ventricular ejection fraction during pregnancy have not been performed in a careful study.

Although further study is necessary to explain conflicting data from various studies and to address certain untested possibilities, it appears that pregnancy is generally not a consideration when evaluating data obtained from invasive hemodynamic monitors.

PULMONARY CONSIDERATIONS AND MECHANICAL VENTILATION

Airway protection is a concern in the pregnant patient. By 20 weeks gestation, the hormonal changes of pregnancy and the enlarging gravid uterus lead to reduced gastric emptying and a greater risk of pulmonary aspiration.[28] In situations in which the level of consciousness is depressed, the trachea should be intubated with a cuffed endotracheal tube to decrease the risk of aspiration.

The airway mucosa undergoes capillary engorgement during pregnancy, leading to a decrease in upper airway and tracheal diameter. This narrowing can easily be exacerbated by other insults, such as inhalation injury or trauma, and the trachea may need to be intubated to preserve airway patency in situations that normally would be followed by a longer period of observation.

It is important to place an endotracheal tube with as large an internal diameter as possible to avoid the increased work of breathing resulting from high airway resistance. In women, a 7.0- or 8.0-mm internal diameter endotracheal tube is often used. The airway mucosal swelling may permit only the nasal passage of a smaller endotracheal tube (for example, 6.5-mm internal diameter) and may predispose to epistaxis, particularly if topical vasoconstrictors are not employed. The smaller endotracheal tubes should also be available for oral intubation, especially in the preeclamptic patient, in whom upper airway narrowing may be pronounced. Once an airway is established, the type of pulmonary disease in conjunction with the physiology of pregnancy must be considered for appropriate pulmonary therapy.

The pregnant patient experiences changes in pulmonary physiology that may impact the diagnosis and treatment of pulmonary disease in the ICU. Ventilation in the pregnant patient is affected by the metabolic and anatomic changes of pregnancy. Minute ventilation is increased with pregnancy as a result of increased CO_2 production[28] and the maintenance of a $Paco_2$ of approximately 32 torr. This hyperventilation occurs in the presence of a 45% decrease in total compliance, which is secondary to a decrease in extrapulmonary (thoracoabdominal) compliance attributed to uterine enlargement and elevation of the diaphragm. Lung compliance remains normal. Airway resistance in the pregnant patient is unchanged or is slightly decreased by the bronchodilating effects of progesterone. By relating the increased ventilatory requirement to the possible increased work of breathing, the pregnant patient is left with a smaller ventilatory reserve than the nonpregnant patient. Difficulty handling the increased ventilatory load of superimposed pulmonary disease may be the result of this situation.

Although superimposed disease will influence the appropriate $Paco_2$ and pH for the patient, there are consequences to hypocarbia and hypercarbia in the pregnant patient. Hypocarbia (below 32 torr) can increase uterine vascular resistance and decrease uteroplacental blood flow. Furthermore, the alkalosis can shift the oxyhemoglobin dissociation curve to the left and decrease oxygen unloading to the fetus. Hypercarbia can lead to fetal acidosis and myocardial depression, and chronic hypercarbia has been shown to produce fetal anomalies in rats and rabbits.

Pulmonary oxygenation in the pregnant patient may be impaired secondary to changes produced in the relationship between closing capacity and functional residual capacity (FRC). The enlarging uterus leads to diaphragmatic elevation, which causes a reduction in FRC relative to closing capacity, especially in the supine position. This may result in airway closure during normal tidal ventilation and can predispose the patient to atelectasis. Ventilation-perfusion abnormalities and a widened $P(A\text{-}a)O_2$ gradient may occur. The pregnant patient is more vulnerable to rapid hemoglobin desaturation and hypoxemia with superimposed pulmonary disease in view of the decreased FRC and increased oxygen consumption as baseline.

Maternal needs should determine the appropriate inspired oxygen concentration. It is important to realize that high inspired oxygen concentrations are not deleterious to the fetus, and will not cause retrolental fibroplasia or premature closure of the ductus arteriosis.[28] Placental shunting will prevent fetal Pao_2 from exceeding 60 torr when maternal Pao_2 is 600 torr. However, hyperbaric oxygen administration has been shown to produce retrolental fibroplasia and other fetal anomalies in rabbits and therefore, the benefit of this therapy to the mother must be weighed against the potential risk to the fetus.[7]

Although numerous factors will influence the ventilator settings, it is important to consider the effect of airway pressure on intrathoracic pressure. Increased intrathoracic pressure will reduce venous return and cardiac output by a number of mechanisms. The degree of reduction in cardiac output is primarily a function of airway pressures, compliances (pulmonary, thoracoabdominal), and the intravascular volume state. The additive effect of increased intrathoracic pressure and caval compression in the pregnant patient may have profound hemodynamic consequences, particularly in a hypovolemic situation. Increased intrathoracic pressure can also reduce uteroplacental blood flow by increasing uterine venous pressure.

The reduced thoracoabdominal compliance of pregnancy, when coupled with the decreased pulmonary compliance of acute lung injury, will translate into higher airway pressures during mechanical ventilation. Barotrauma risk is subsequently increased, particularly in the acid aspiration syndrome.[10]

Patients receiving positive-pressure ventilation are often placed in a head-up position in order to improve V/Q matching and thereby decrease dead space ventilation. Furthermore, this position will result in less compression of the diaphragm by the abdominal viscera which may lead to an increase in FRC. In the supine position, increased perfusion in the dependent portion of the lung is combined with preferential ventilation of the nondependent portion leading to V/Q mismatching.

These positioning considerations are important in the mechanically ventilated obstetric patient. The 30- to 45-degree head-up position in the obstetric patient may also improve thoracoabdominal compliance by decreasing the pressure of the enlarged uterus on the thorax. Yet, at the same time, the head-up position, combined with positive-pressure ventilation and inferior vena cava compression by the uterus, can lead to a severe reduction in venous return. For this reason, the mechanically ventilated pregnant patient must always have left uterine displacement, with the head-up position instituted according to the hemodynamic situation. The lateral position may be beneficial in improving Pa_{O_2} in certain inhomogeneous (for example, unilateral) disease processes and will prevent inferior vena cava compression.

PULMONARY MANAGEMENT MEDICATIONS

Pregnant patients with reversible obstructive lung disease may require treatment with bronchodilators and steroids. Subcutaneous epinephrine and terbutaline are reported as being equally effective in these patients.[33] In early pregnancy, terbutaline may be preferred because of a reported increase in fetal malformations with repeated doses of epinephrine.[14] In late pregnancy, the situation is more complex because epinephrine has adverse effects on uterine blood flow, and terbutaline has been associated with pulmonary edema in this patient population.[2] Inhaled bronchodilators, which produce less systemic response than subcutaneous therapy and some of which are more specific β_2 agonists (for example, albuterol), have been used frequently during pregnancy, but there are no data regarding the safety of these drugs in the pregnant population.

An association between theophylline and fetal malformations has been demonstrated in laboratory animals with large doses,[31] but it is generally agreed that theophylline preparations can be used safely during pregnancy.[15] The requirement for theophylline will increase as pregnancy progresses secondary to an increased volume of distribution. However, with the weight gain during pregnancy, dosage on a milligram per kilogram basis does not change significantly.[28] It is recommended that theophylline levels remain in the low therapeutic range (10 to 14 mg per mL). Both theophylline and β-agonists decrease uterine contractility and slow the progress of labor.

Steroids have been associated with intrauterine growth retardation in humans and congenital abnormalities in laboratory animals,[19,30] but studies have demonstrated that oral corticosteroids can be used safely in pregnant patients with asthma.[23] It is recommended that steroids be used sparingly in pregnant patients, employing the lowest effective dose.

Muscle relaxants are occasionally employed in mechanically ventilated patients. They may predispose the patient to venous thrombus formation by increasing venous stasis, and in the pregnant patient, thromboembolic phenomena may be a significant concern. Additionally, muscle relaxants may pose a threat to the fetus. Long-term administration of pancuronium in animals has been associated with joint malformations in the fetus secondary to immobilization in utero.[21] Furthermore, muscle relaxants do not easily cross the placenta because of their polar structure, but prolonged use may lead to fetal accumulation and apnea at birth.

Sedatives are often used to increase the tolerance for mechanical ventilation and the fetal effects of these drugs must be considered. Of the benzodiazepines, diazepam has been associated with an increased risk of cleft lip or palate in offspring, especially if used in the first and second trimester.[4] Other congenital defects have been associated with diazepam and, although some studies report no association of birth defects with the drug, it should probably not be used. Lorazepam has not been associated with any congenital defects to date[4]; however, the experience with the drug is not great.

The use of pentobarbital and secobarbital in pregnant patients has not been linked with any congenital defects.[4] Hemorrhagic disease of the newborn and barbiturate withdrawal have been reported to be theoretical possibilities.

The use of narcotics such as morphine and fentanyl has not been associated with any congenital defects.[4] Maternal addiction to narcotics can lead to neonatal withdrawal, and this must be a concern when using large doses of any narcotic for an extended period.

CONCLUSION

The critical care management of the pregnant patient has been discussed, with particular emphasis placed on the physiology of pregnancy as it relates to intensive therapy. Although the literature on this topic is not extensive, appropriate clinical decisions can be made by applying a knowledge of the physiologic changes that occur during pregnancy to common management situations in the ICU. Moreover, it is important to remember that two patients, the mother and the fetus, require attention when therapy is instituted in the critically ill pregnant patient.

REFERENCES

1. Bader RA, Bader ME, et al: Hemodynamics at rest and during exercise in normal pregnancy as studied by cardiac catheterization. J Clin Invest 34:1524, 1955
2. Benedetti TJ: Maternal complications of parenteral beta-sympathomimetic therapy for premature labor. Am J Obstet Gynecol 145:1–7, 1983
3. Blanchard K, Dandavino A, et al: Systemic and uterine hemodynamic responses to dopamine in pregnant and nonpregnant sheep. Am J Obstet Gynecol 130:669–673, 1978
4. Briggs G, Bodendorfer T, et al (eds): *In* Drugs in Pregnancy and Lactation. Baltimore, Williams & Wilkins, 1983, pp 109, 140, 201, 236, 271, 328
5. Cotton DB, Bernstein SG, et al: Hemodynamic observations in evacuation of molar pregnancy. Am J Obstet Gynecol 138:6–10, 1980
6. Cotton DB, Gonik B, et al: Cardiovascular alterations in severe pregnancy induced hypertension: Relationship of central venous pressure to pulmonary capillary wedge pressure. Am J Obstet Gynecol 151:762–764, 1985
7. Fujikara T: Retrolental fibroplasia and prematurity in newborn rabbits induced by maternal hyperoxia. Am J Obstet Gynecol 90:854–858, 1964
8. Goldfarb G, Lebrec D: Percutaneous cannulation of the internal jugular vein in patients with coagulopathies: An experience based on 1000 attempts. Anesthesiology 56:321–323, 1982
9. Greiss FC, Pick JR: The uterine vascular bed: Adrenergic receptors. Obstet Gynecol 23:209–213, 1964
10. Haake R, Schlichtig R, et al: Barotrauma. Chest 91:608–612, 1987
11. Levinson G, Shnider SM, et al: Effects of maternal hyperventilation on uterine blood flow and fetal oxygenation and acid-base status. Anesthesiology 40:340, 1974
12. Motoyama EK, Acheson RG, et al: Adverse effect of maternal hyperventilation on the foetus. Lancet 1:286–288, 1966
13. Naulty J, Cefalo RC, et al: Fetal toxicity of nitroprusside in the pregnant ewe. Am J Obstet Gynecol 139:708–711, 1981
14. Niederman MS, Matthay RA: Asthma and other severe respiratory diseases during pregnancy. *In* Berkowitz RL (ed): Critical Care of the Obstetric Patient, New York, Churchill Livingstone, 1983, pp 335–366
15. Pollowitz JA: Theophylline therapy during pregnancy. JAMA 243:651–652, 1980
16. Rafferty TD, Berkowitz RL: Complications of pulmonary artery catheterization in obstetric patients. Int J Gynaecol Obstet 18:133–135, 1980
17. Rafferty DT, Berkowitz RL: Hemodynamics in patients with severe toxemia during labor and delivery. Am J Obstet Gynecol 138:263–270, 1980
18. Ralston DH, Shnider SM, et al: Effects of equipotent ephedrine, metaraminol, mephentermine, and methoxamine on uterine blood flow in the pregnant ewe. Anesthesiology 40:354–370, 1974
19. Reinisch JM, Simon NG, et al: Prenatal exposure to prednisone in humans and animals retards intrauterine growth. Science 202:436–438, 1978
20. Ring G, Krames E, et al: Comparison of nitroprusside and hydralazine in hypertensive pregnant ewes. Obstet Gynecol 51:598–602, 1977
21. Roizen MF, Feely TW: Pancuronium bromide. Ann Intern Med 88:64–68, 1978

22. Rolbin SH, Levinson G, et al: Dopamine treatment of spinal hypotension decreases uterine blood flow in the pregnant ewe. Anesthesiology 51:36–40, 1979
23. Schatz M, Patterson R, et al: Corticosteroid therapy for the pregnant asthmatic patient. JAMA 233:804–807, 1975
24. Secher NJ, Arnsbo P, et al: Haemodynamic effects of oxytocin and methylergometrine on the systemic and pulmonary circulations of pregnant anaesthetized women. Acta Obstet Gynecol Scand 57:97–103, 1978
25. Secher NJ, Anderson LH: Changes in the pattern of regional pulmonary blood flow after PGF2-alpha in pregnant women. Cardiovasc Res 11:26–30, 1976
26. Seneff MG: Central venous catheterization: A comprehensive review, part I. J Intensive Care Med 2:163–175, 1987
27. Seneff MG: Central venous catheterization: A comprehensive review, part II. J Intensive Care Med 2:218–232, 1987
28. Shnider SM, Levinson G: Anesthesia for Obstetrics. Baltimore, Williams & Wilkins, 1987, pp 3–8, 10, 199, 280
29. Snyder SW, Wheeler AS, et al: The use of nitroglycerin to control severe hypertension of pregnancy during cesarean section. Anesthesiology 51:563–564, 1979
30. Warrel DW, Taylor R: Outcome for the fetus of mothers receiving prednisolone during pregnancy. Lancet 1:117–118, 1968
31. Weinberger SE, Weiss ST, et al: Pregnancy and the lung. Am Rev Respir Dis 121:559–581, 1980
32. Wheeler AS, James FM III, et al: Effects of nitroglycerin and nitroprusside on the uterine vasculature of gravid ewes. Anesthesiology 52:390–394, 1980
33. Wilson AF: Drug treatment of acute asthma. JAMA 237:1141–1143, 1977

Address reprint requests to

Ronald Dworkin, MD
Department of Anesthesiology
Greater Baltimore Medical Center
6701 North Charles Street
Baltimore, MD 21204

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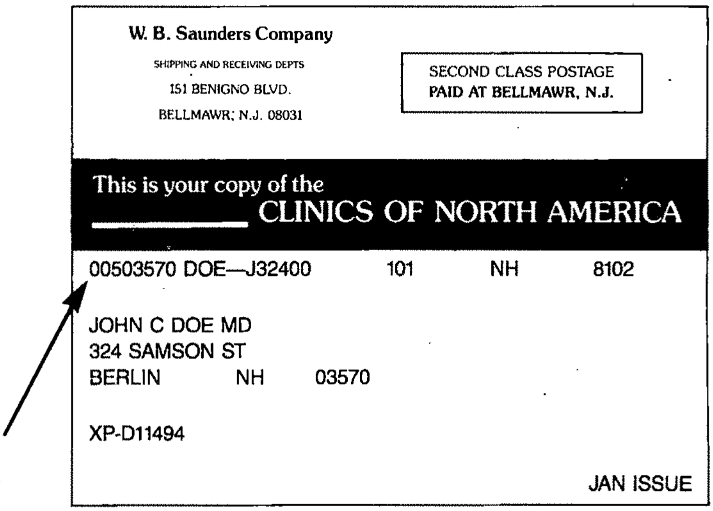

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